

Research and Clinical Aspects of the Late Effects of Poliomyelitis

Editors

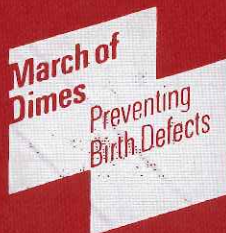
Lauro S. Halstead, MD

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Birth Defects:

Original Article Series

Volume 23, Number 4, 1987



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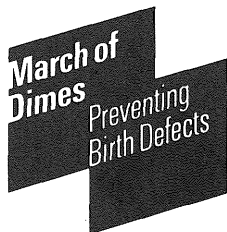
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FROM THE SECOND RESEARCH SYMPOSIUM on the LATE EFFECTS OF POLIOMYELITIS

Sponsored By

GEORGIA DIVISION OF REHABILITATION SERVICES,
DEPARTMENT OF HUMAN RESOURCES,

ROOSEVELT WARM SPRINGS INSTITUTE FOR REHABILITATION,
Warm Springs, Georgia

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RESEARCH AND CLINICAL ASPECTS OF THE LATE EFFECTS OF POLIOMYELITIS

Second Research Symposium on the Late Effects of Poliomyelitis
Warm Springs, Georgia—September 5–7, 1986

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INTRODUCTION

The story of the late sequelae of polio is a fascinating one. The first descriptions that we know of appeared in 1875 when three patients were reported in the French literature. All three cases involved young men who had a history of paralytic polio in infancy and then, many years later, as young adults, developed significant new weakness and atrophy. What is of particular interest in these cases, is that the weakness and atrophy occurred not only in previously affected but, in at least two instances, previously unaffected muscles. In addition, all of the subjects had physically demanding jobs that required strength and endurance.

In a commentary on one of the cases, the great French neuropathologist Jean Martin Charcot suggested several hypotheses for these changes, which are still relevant today. He believed that a previous disease of the spinal cord—in this case, polio—might leave a patient more susceptible to a subsequent spinal disorder and that the new weakness was due to overuse of the uninvolved limbs.

Since this first burst of interest over 100 years ago, there have been sporadic case reports but, by and large, the late sequelae of polio have remained an obscure and largely unexplained corner of medicine until recently. Why this relative neglect occurred is not entirely clear. After all, few diseases are as widely prevalent in the world and have been as intensively investigated. Part of the explanation may lie in the fact that over the years, polio has been viewed as a classic example of an acute viral infectious disease. Therefore, most of the energy and resources were directed at early management and prevention. Following widespread use of the vaccines, polio quickly became a medical oddity in the industrialized world, and interest and funding in polio-related problems waned. Part of the explanation may also lie in the fact that the big epidemics in this century did not occur until the 1940s and 1950s. These individuals are 30 to 40 years post-onset when new neurologic changes tend to appear. Thus, many thousands of polio survivors are now experiencing new problems related to polio and by sheer weight of numbers, are finally attracting attention among the medical and lay communities.

In response to these perceived “new” health problems, the first Research Symposium on the Late Effects of Polio was held in May 1984 at Warm Springs, Georgia. The major agenda for that conference was to clarify the nature and extent of the new problems, discuss the most likely hypotheses for the underlying causes, develop a rational basis for treatment, and identify the major research questions that needed to be addressed in the coming years.

In retrospect, it was an ambitious agenda—especially for a 2½ day

conference that was organized in less than 12 months. However, it is now clear the time was historically ripe for such a meeting. In addition to the numerous support groups of polio survivors that were developing all over the country and clamoring for help and information, a growing number of clinicians and researchers were becoming aware that their old concepts about polio as a static neurologic disease were no longer valid and that a fresh look into the pathology and treatment of polio sequelae was required. Although a good deal of information was presented and discussed at the first symposium, no issues were settled conclusively and more questions were raised than answered. Indeed, the major conclusion of that meeting was the urgent need for more research and the major impact was to provide a heightened awareness in the medical and lay communities of the existence and importance of the late complications of polio. And finally, the major recommendation of the first meeting was to hold a second research symposium as a way of helping to sustain the momentum that was initiated in 1984 and to provide a state-of-the-art review concerning research and management issues. These proceedings are a tangible result of that recommendation and represent the next chapter in the unfinished story of the late sequelae of polio.

The Second Research Symposium on the Late Effects of Polio was held September 5-7, 1986 in Warm Springs, Georgia. Attendees included nearly 50 invited scientists and clinicians from 7 countries who gathered for an informal series of presentations, discussion, and comradery that extended over 2½ days in the beautiful and historic setting of the Roosevelt Warm Springs Rehabilitation Institute in rural Georgia. Our hope with these proceedings, as with those published from the first symposium, is that they will provide an important source of information for medical professionals, polio survivors, and others concerned about the late effects of polio. In addition, it is hoped that they will serve as a continuing catalyst to stimulate more research, initiate new clinical services, and help generate funding to support the resources needed to gain a better understanding of this medical problem.

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Late Effects of Polio: Historical Perspectives

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The possibility of a second or late progression of weakness and atrophy after the initial attack of poliomyelitis is not a new concept. It was actually set forth in the 19th century at a time when the exact cause of polio was unknown, and very little was known about the course or treatment of myelitis and encephalitis. The last quarter of the 19th century was, however, a time of great interest in the study of the nervous system and its function.

Probably the first explanation for the late effects of polio was offered by Dr. Jean Martin Charcot, a professor of pathology and neurology at Salpêtrière Hospital in Paris. Charcot felt that a previous disease of the spinal cord rendered a patient more susceptible to a subsequent spinal disorder [1]. In 1875, Raymond [1], who was a colleague of Charcot, presented an unusual case before the Society of Biology in Paris. The patient was a 19-year-old tanner who presented to Dr. Raymond with a history of progressive muscular atrophy involving the right arm and leg as well as an old left hemiparesis. He had apparently suffered the sudden onset of fever, convulsions, and left arm and leg paralysis at the age of 6 months. By the age of 7 years, the patient had regained partial use of his left arm and leg. As a young man, his work as a tanner required great effort with his right arm. At the age of 17, he began to complain of fatigue and heaviness in this limb. In a short time, weakness and atrophy developed in the right arm and subsequently in the right leg. Charcot attributed the left hemiparesis to poliomyelitis, and the late onset of right-sided weakness to overuse, resulting in an extension of the lesion from the left to the right anterior horn of the spine. Whether or not this patient really had polio or some other encephalomyelitis remains unknown, but the first concept of the late effects of polio had been proposed.

Later in that same year, Cornil and Lepine [2] reported the case of a 27-year-old man who had had poliomyelitis as an infant. Although both lower limbs were affected, the patient completely recovered. As a soldier during the Franco-Prussian war, this man was subjected to prolonged marches and overexertion, and his right leg became weak. This weakness progressed, and 8

months later, the left leg became weak and both legs began to show significant atrophy. Several years later, weakness and atrophy developed in both arms.

Two other cases were reported in the medical literature in 1875 by Carriere [3] involving progressive muscle weakness and atrophy following a previous attack of poliomyelitis. The first case was that of an 18-year-old carrier who had had poliomyelitis involving all 4 limbs, but primarily the arms, at the age of 6 months. His recovery was generally good, but residual weakness remained in the arms. This man's work involved repetitive use of the arms, and at the age of 16, the muscles of the right shoulder and arm began to atrophy and weaken. Carriere diagnosed the condition as progressive muscular atrophy. The second case in 1875 was that of a 16-year-old boy who had had poliomyelitis at the age of 6 months resulting in paraplegia. At the age of 15, his legs gradually became weaker with involvement of the arms over the next several months. Carriere felt that this patient had amyotrophic lateral sclerosis.

Four years later, in 1879, eight case reports of progressive muscular weakness and atrophy following a previous episode of poliomyelitis appeared in the medical literature [4–6]. Vulpian [7], a close associate of Charcot, reported a case along with the first autopsy report. The patient was a girl who had had poliomyelitis at 3½ years of age resulting in incomplete paralysis of the lower limbs. The leg weakness began to increase at the age of 15 and was followed by weakness of the arms. The patient subsequently died, and examination of the spinal cord revealed periependymal myelitis with loss of cells in the anterior horn. Those anterior horn cells that were present demonstrated foci of different degrees of degeneration.

The first reports of progressive post-polio changes in the German literature were by Seeligmüller [8] who, in 1879, reported 4 different cases. The first was a boy who had had poliomyelitis at the age of 3, leaving the left leg atrophied and weak. The patient presented at age 18 with progressive weakness and atrophy in the previously unaffected right leg. The second case was that of a 29-year-old school teacher who had had poliomyelitis in infancy affecting the right shoulder muscles. At the age of 28, following intoxication and exposure to cold, this patient's right arm became weak and subsequently atrophied. The third case was that of a 26-year-old merchant whose left leg had been paretic since childhood due to poliomyelitis. At the age of 17, he began to notice that his left leg was becoming weaker and that the right leg was beginning to atrophy. By the age of 26, both thigh muscles were starting to atrophy. Seeligmüller's fourth case report was a 26-year-old hatter who had had poliomyelitis at age 5 with residual weakness of the left shoulder. When he was 15 years old, these same left shoulder muscles became weaker and as time went on, they continued to atrophy and eventually became nonfunctional.

By the close of the 19th century, approximately 20 more case reports appeared in the European literature questioning the relationship between a previous attack of poliomyelitis and a second disorder of the spine [9–24] (Table 1).

The first reports in the English language came in 1899. Sir William Gowers [23], in the 1899 edition of his textbook of neurology, reported 2 cases of lateral sclerosis that developed in patients previously affected by poliomyelitis. He stated that he felt the secondary disorder was a myelitis instead of a primary neuron disorder. On February 7, 1899, William Hirsch [24] read a paper entitled “On the Relations of Infantile Spinal Paralysis to Spinal Diseases of Later Life” to the New York Neurological Society. In this paper, he reviewed the 19th century literature and stressed the importance of considering in further studies only those cases without sensory symptoms and a pure motor disorder that could be classified as progressive muscular atrophy. He noted 3 classes: those in whom the secondary weakness occurred in the previously affected muscles, those in whom the secondary weakness developed in previously unaffected muscles, and those in whom the secondary weakness developed in both.

Hirsch [24], in his review of the 19th century literature, felt 3 basic diagnostic theories had been proposed. The first was that irritation of the cord by the old lesion enfeebled it and made it a “locus minoris resistentiae” which, on occasion, might become susceptible to further disease. The second theory

TABLE 1. Case Reports From the 19th Century

1875	1882	1893
Raymond and Charcot (1) [1]	Landouzy and Déjérine (1) [15]	Grandan (1) [13]
Cornil and Lepine (1) [2]		Déjérine (1) [11]
Carriere (2) [3]	1884	Bernheim (1) [10]
	Ballet and Dutil (3) [9]	
1879		1894
Vulpian (1) [7]	1886	Laehr (1) [14]
Hayem (1) [5]	Thomas (2) [22]	
Seeligmuller (4) [8]		1896
Quinquaud (1) [6]	1888	Langer (1) [16]
Caudoin (1) [4]	Dutil (1) [12]	
		1899
1881	1890	Hirsch (1) [24]
Oulmont and Neumann (2) [19]	Rendu (1) [20]	Leszynsky (1) [17]
	Nenninger (1) [18]	Gowers (2) [23]
	1891	
	Sterne (2) [21]	

() = No. of case(s)

[] = Reference

expressed by Charcot postulated that in some individuals there was a certain disposition of vulnerability, which at some period in their lives could give rise to polio and at other times progressive muscular atrophy. The third view theorized that the initial inflammatory process resulted in scarring, forming a latent but permanent focus that could flare up at a later date.

William Hirsch [24] went on to describe a case of a tailor who had poliomyelitis at 2 years of age, leaving him with weakness of the left upper limb. At age 42, he developed stiffness and weakness of the legs. Atrophy and weakness developed in the muscles of the trunk and both upper limbs. He developed upper motor neuron signs and was diagnosed as having amyotrophic lateral sclerosis. Swallowing difficulties developed and the patient subsequently died. Postmortem examination revealed a myelitis and not a primary neuron disease.

The first major review in this country of the late effects of polio was conducted by Charles Potts [25] at the University of Pennsylvania in 1903, citing 36 cases in the literature from the time of Charcot. Potts felt that on the basis of the data given, the second condition in 28 of the 36 cases could be diagnosed as progressive muscular atrophy. Two of the cases could be diagnosed as amyotrophic lateral sclerosis, and 2 cases as myelitis. He felt that the remaining 4 cases were due to a second attack of poliomyelitis. In these cases, the time between the initial attack of polio and the second condition was 7 to 55 years, with an average of about 23 years. Where it could be determined, in 18 of the 33 cases, the secondary atrophy began in a limb that had previously been affected.

Kaumheimer [26], a German physician, in 1920 reported on 48 cases of progressive muscular atrophy in patients who had previously had poliomyelitis. The next major review of the topic was in 1936, when a paper by Leon Salmon and Henry Riley [27] was published in the *Bulletin of the Neurological Institute of New York*, including a description of 3 of their own cases. They found over 60 cases with progressive spinal muscular atrophy or what was referred to as chronic anterior poliomyelitis occurring as a secondary condition following a previous attack of poliomyelitis. In their review, they found only 6 cases of amyotrophic lateral sclerosis, 2 cases of myelitis, and 2 cases of transitory paresis or paralysis following a previous attack of poliomyelitis. This work of Salmon and Riley strengthened the belief in the clinical association between poliomyelitis and progressive muscular atrophy. They believed that an association between previous poliomyelitis and amyotrophic lateral sclerosis was unlikely and probably coincidental. In trying to explain the occurrence of the second disorder, they theorized that "the virus or whatever it is that causes the manifestations of acute anterior poliomyelitis may affect only slightly certain nerve cells or even lie dormant in the nervous

system for an indefinite length of time and only at some later date make its presence known.”

Isolated cases continued to appear in the medical literature throughout the mid-20th century. In 1952, Geiger [28] reviewed 11 cases reported from 1910 to 1952, primarily from the German literature and added 2 more cases of his own. Despite all these case reports, there were many problems in attempting to evaluate these early studies. Prior to this time, the diagnosis of poliomyelitis was purely clinical, and some of the reported cases may have had other non-polio encephalomyelitic conditions. Also, very few of these reports cited any long-term follow-up and the final outcome of these cases remains unknown. It is also of interest that almost all of these patients acquired polio in infancy or early childhood.

The experience of the English at the National Hospital, Queen Square, was published in 1962. Zilkha [29] reported on the long-term survival of 11 patients with progressive muscular atrophy who had a previous history of poliomyelitis. Five of these patients had extensor plantar responses, but none had bulbar symptoms or signs. Of these 11 patients, one died from a new illness and the other 10 showed varying degrees of deterioration. One patient was 11 years post-onset of a new weakness. Zilkha [29] stressed the benign nature of this secondary condition in this first study to evaluate long-term progression of weakness.

In 1964, Pinelli and Ramelli [30] reported a case in which they felt the anterior spinal nerve roots and not the motor neurons were compromised. They pointed to the effect of previous polio on poor vertebral alignment and scoliosis and the resultant unphysiologic posture. They reviewed the literature and grouped the existing theories into 5 major concepts as to the origin of the secondary onset of weakness. The first hypothesis was that the late progressive muscular atrophy was purely coincidental. The second was that the acute poliomyelitis produced an acquired predisposition to the late muscular atrophy by causing a “locus minoris resistentiae.” The third hypothesis was that there was an endogenous predisposition of the cord to certain diseases such as polio and progressive muscular atrophy. The fourth theory was that a discrepancy existed between demands and functional capacity of the anterior horn cells due to increased motor unit territory. The fifth theory postulated that the late onset of muscular atrophy was due to recrudescence of a latent viral infection.

Poskanzer, Cantor, and Kaplan [31] attempted to calculate the frequency by chance of previous poliomyelitis in amyotrophic lateral sclerosis. Using data from the Massachusetts General Hospital between 1937 and 1966, they calculated that by chance, one case of prior poliomyelitis would be expected in 353 cases of amyotrophic lateral sclerosis. Their actual data,

however, documented 5 cases with a previous attack of poliomyelitis among 196 patients with amyotrophic lateral sclerosis, raising the possibility that the 2 disorders are related.

In 1969, Campbell, Williams, and Pearce [32] presented 5 cases and stressed the benign nature of the disorder. They reviewed the literature of 83 other cases and suggested the possible role of a severe scoliosis compromising the cord or spinal nerve roots as a factor in the late onset of weakness.

In 1970, Hamilton, Nichols, and Tait [33] presented a paper focusing on the respiratory and circulatory insufficiency of late-onset weakness after polio. They presented 14 cases and demonstrated the development of insidious problems over many years. They recommended treatment with a portable intermittent positive-pressure respirator for 5 to 15 minutes, 3 to 6 times a day with the use of more conventional respiratory aids at night. They felt that the severity of late-onset respiratory and circulatory insufficiency was most likely to occur in those patients who had initially suffered severe respiratory impairment or severe involvement of all 4 limbs. They also felt that those patients who developed acute poliomyelitis later in life, and those highly motivated patients who pushed themselves beyond the competence of their respiratory and circulatory systems were also most likely to develop problems.

In 1972, Mulder, Rosenbaum, and Layton [34] reported the experience of the Mayo Clinic; 34 patients had been followed from 1942 to 1970. Six of these patients had extensor plantar responses. All patients had progression of weakness and most noted continued muscle fasciculations and atrophy. Those patients in this study who developed late-onset weakness were few in number compared to the total number of polio patients who had been severely affected by polio in childhood, the median age of onset being 5 years. The secondary weakness then occurred at an average of 37 years post-onset. The relatively benign, slowly progressive nature, and minimal evidence of lateral-column signs differentiated these patients from those with amyotrophic lateral sclerosis. They pointed out that in their studies, as well as others, men appear to be more frequently affected than women.

Additional case reports have continued to appear in both the German and American medical literature [35] (Table 2). There appears to be agreement about an association between the late onset of progressive muscle weakness and a previous attack of poliomyelitis. This late-onset weakness generally occurred 30 to 40 years post-poliomyelitis but was seen as late as 70 to 75 years and as early as 5 to 10 years post-poliomyelitis. The disorder was of a more benign nature, affecting the motor neuron, and clinically resembled progressive muscular atrophy. The relative lack of lateral column signs and its slow progressive course differentiated it from classic amyotrophic lateral sclerosis. It was, however, accepted that by coincidence, an occasional old

TABLE 2. Case Reports From the 20th Century

Date	Cases Reviewed	Reviewer [Reference]
1903	36	Potts [25]
1920	48	Kaumheimer [26]
1936	3	Salmon and Riley [27]
1952	13	Geiger [28]
1962	11	Zilkha [29]
1964	1	Pinelli and Ramelli [30]
1969	5	Campbell et al [32]
1970	14	Hamilton et al [33]
1972	34	Mulder et al [34]
1973	4	Kayser-Gatchalian [35]

polio patient would acquire amyotrophic lateral sclerosis. The possibility that scoliosis or other postural abnormalities might lead to spinal nerve root compromise or spinal cord compression was a recurring consideration in the evaluation of these patients. The late-onset weakness seemed to occur in relatively few of the post-polio patients.

In the late 1970s, Wiechers and Hubbell [36] began employing single fiber electromyography (EMG) to study the physiology of the reinnervated motor unit. We began by looking at older post-polio patients who were not having problems of progressive muscular atrophy. To our surprise, we found that even in normal or Grade G ($\frac{4}{5}$ MRC) muscles, there were large reinnervated motor units having transmission abnormalities in asymptomatic post-polio patients. This transmission abnormality appeared to be a nerve terminal problem. The single fiber examination of weak muscles of less than antigravity strength demonstrated profound neuromuscular transmission abnormalities in almost every surviving motor unit. This led to our study [36] of normal or Grade G ($\frac{4}{5}$ MRC) strength muscles in post-polio patients of various ages who were not experiencing problems. We proposed the concept of the peripheral disintegration of the reinnervated motor unit. In another study by Halstead and co-workers [37] during 1983–84, questionnaires were distributed to groups of post-polio patients. The reports seemed to confirm the fact that many more post-polio patients were having problems with fatigue, progressive weakness, and loss of function than would be surmised by the relatively few case reports in the medical literature.

Dalakas and others [38] at the National Institutes of Health followed a group of post-polio patients who were having new progressive muscular atrophy but no evidence of lateral column disorders. The 27 patients studied were stable for at least 15 years prior to the onset of new weakness. All were less than 60 years of age and experienced slowly progressive weakness that varied from patient to patient. Biopsy data revealed several isolated atrophic angulated fibers that stained darkly with an enzymatic reaction characteriz-

ing them as new active denervation. No group atrophy characteristic of recent motor neuron death was seen. Single fiber EMG studies on these patients confirmed transmission abnormalities at the site of the neuromuscular junction. They concluded that the site of compromise in late-onset weakness following poliomyelitis was at the individual nerve terminal with the falling off of individual muscle fibers. The spinal fluid of 7 of the 13 patients studied had 2 to 4 oligoclonal IgG bands. The total IgG, the IgG index, and IgG synthesis were normal. In 12 of 27 biopsies, occasional small perimysial or perivascular lymphocytic infiltrates were observed. These latter 2 findings leave questions as to the role of virologic or immunologic mechanisms in late-onset progressive muscular weakness following polio.

Two terms have become commonplace to describe these problems. The term "post-polio syndrome" is used in a general sense to describe those conditions that are the direct effects of progressive muscle weakness or the indirect result of the late effects of polio. These indirect effects include the early development of degenerative arthritis in a joint that is biomechanically disadvantaged and wears abnormally due to muscular imbalance. Psychologic and social problems of long-term disability and learning to deal with a new progressive disorder after a long period of stability are also an indirect result and part of the post-polio syndrome. New back pain as a result of a progressive scoliosis and deterioration of pulmonary function are also examples of direct or indirect results of the late effects of polio.

The term "progressive post-polio muscular atrophy" (PPMA) is a part of the post-polio syndrome. It is used to describe those patients who have a direct and demonstrable late progression of muscle weakness, frequently with new atrophy involving muscles that had been previously affected or clinically unaffected by the original disease, for which there are no other neuromuscular causes, and in whom there is no evidence of a concurrent upper motor neuron disorder. The diagnosis of PPMA is a diagnosis of exclusion. The presence of upper motor neuron signs such as the Babinski reflex or spasticity precludes the diagnosis of PPMA. A search for spinal cord compromise or the rare occurrence of ALS, multiple sclerosis, or other upper motor neuron disorders superimposed upon the residuals of polio should be undertaken.

Since the first research symposium on the late effects of polio in 1984, much work has been started. The public has become aware of the post-polio syndrome. Post-polio survivor groups have begun to develop throughout this country and other countries demanding greater understanding, increased medical knowledge, and support. Gini Laurie and her long-standing post-polio support group and *Rehabilitation Gazette* have become the rallying focus for many post-polio organizations.

At the beginning of the second research symposium on the late effects of polio, several major questions remained to be answered.

- 1) What is causing the transmission abnormalities in the post-polio reinnervated motor unit? If it is an inability to keep pace with the metabolic demand of all of its muscle fibers, what is the underlying problem? Is the cell body scarred from the previous polio? Has the hyperfunctioning motor neuron simply worn out or is there a viral or immunologic mechanism affecting the motor neuron's continued function?
- 2) Since the transmission abnormality seems to be present in all post-polio patients, why do only some patients complain of new problems?
- 3) Is there anything that can be done to boost the motor neuron's metabolic function without causing its early demise?
- 4) Will exercising the muscle help to regain strength, or, with time, only increase the demand on the motor neuron or nerve terminals and result in earlier compromise?
- 5) What role does overexertion or vigorous activity play in precipitating sudden weakness? Does it result in the sudden death of a few large reinnervated motor neurons or do the neuromuscular junctions just fatigue to a nonrecoverable state? Does physical breakage of axon sprouts occur with vigorous activity?
- 6) How can we best treat these patients today?

Hopefully, new ideas will be developed and formulated to help answer some of these basic questions and the many others that will be raised. The problem of the late effects of polio may very well become the working model for other neuromuscular diseases.

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Post-Polio Syndrome: Clinical Experience With 132 Consecutive Outpatients*

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INTRODUCTION

In 1983 and 1984, we undertook 2 separate questionnaire surveys of populations in different parts of the United States in a preliminary effort to clarify the nature and extent of the new health problems being reported by persons with a prior history of poliomyelitis. Both surveys were based on self-selected samples. The first was a group of 201 persons and the results were reported in May 1984 at the First Research Symposium on the Late Effects of Poliomyelitis. The second survey, which used the same questionnaire with minor modifications, described the experiences of another group of 539 polio survivors. While the 2 surveys were different in size and separated in time by 8 to 10 months, the results were strikingly similar. Despite the similarity, however, the results were questionable as the data were based exclusively on self-reports by a group of individuals who had not been examined and in which there was no way to confirm any of the information, including the history of poliomyelitis.

In an effort to avoid the biases inherent in a questionnaire survey, and to clarify further the nature of what is becoming recognized as the post-polio syndrome, we analyzed the clinical experience of all patients with a confirmed history of polio who were examined and treated at a post-polio clinic over a period of one year. In addition to presenting these results, we report on the clinical interventions that were recommended along with a preliminary assessment of the effectiveness of these interventions.

METHODS

An outpatient clinic devoted to the special needs and problems of persons with a history of paralytic poliomyelitis was established at The Institute for

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Rehabilitation and Research in the spring of 1984. Patients were seen by members of an interdisciplinary team, which included a physician or physician's assistant, physical therapist, social worker, and nurse. When indicated, they were also seen by an occupational therapist, a vocational counselor, dietician, or psychologist. For additional medical evaluation, patients were referred to other specialists, which most commonly included a pulmonologist, neurologist, neurosurgeon, or orthopedic surgeon. All patients underwent a standard, comprehensive evaluation with emphasis on three objectives: 1) confirming the diagnosis of paralytic polio, 2) excluding other medical and neurologic conditions that might explain the patient's present health problems and functional limitations, and 3) identifying and initiating effective therapeutic interventions. A typical evaluation consisted of seven components:

- 1) A detailed medical history with special attention to current health problems as well as the extent of initial involvement from polio, the period of recovery, the duration of neurologic and functional stability, and the time of onset of new health problems;
- 2) A physical exam with special emphasis on assessing the musculoskeletal and nervous systems;
- 3) An electromyogram (EMG) and nerve conduction study of selected muscles and nerves;
- 4) A biomechanical and functional evaluation with special attention to orthotic and adaptive equipment needs;
- 5) A basic panel of screening laboratory tests that were supplemented with additional x rays and laboratory studies as indicated by the history and physical examination;
- 6) A psychosocial assessment; and
- 7) Referral to other members of the rehabilitation team or other medical specialists as needed.

The confirmation of paralytic polio was based on 4 criteria: 1) history of acute febrile illness with motor loss and without sensory loss; 2) evidence of paralysis, paresis and/or atrophy on physical examination; 3) changes of chronic denervation compatible with prior anterior horn cell disease on EMG; and 4) original medical records when available. The diagnosis of post-polio syndrome was based on 5 criteria and was essentially a diagnosis by exclusion. The criteria are: 1) a confirmed history of paralytic polio; 2) partial to fairly complete neurologic and functional recovery; 3) a period of neurologic and functional stability of at least 15 years duration; 4) the onset of 2 or more of the following health problems since achieving a period of stability: unaccustomed fatigue, muscle and/or joint pain, new weakness in muscles previously affected and/or unaffected, functional loss, cold intolerance, new atrophy; and 5) no other medical diagnosis to explain these health problems.

The initial evaluation lasted between 2 and 4 hours, depending upon the

complexity of the problems presented. Prior to the first visit, patients were mailed a database form, which was reviewed and checked for accuracy during the course of the evaluation. Patients were scheduled for at least one follow-up appointment at which time the results of tests and any interventions were reviewed and evaluated.

STATISTICAL METHODS

New problems encountered by the respondents were analyzed using a life table technique with censored data to identify patterns of incidence at varying periods post-onset of polio. These patterns were quantified in terms of cumulative conditional probabilities measured in 2-year intervals. Censored data applied to all persons who had not developed a new problem during a specified period or were not at risk for the full extent of that time. With this analytic technique, the median time and standard error refer to the duration in which 50% of the population at risk have encountered the problem.

To test hypotheses regarding differences among levels within various risk factors (eg, age at onset, sex), we employed the generalized Savage (Mantel-Cox) equality of survival curve statistic. This test compares the equality of the incidence levels within a given risk factor at various time intervals. In the tables, "P" values listed reflect the differences between the sets of longitudinal cumulative probabilities of the subgroups tested.

RESULTS

From July 1, 1984 to June 30, 1985, a total of 174 persons were evaluated in the post-polio clinic. A breakdown of the status of these patients is outlined in Table 1. Five patients did not fulfill the criteria for diagnosis of paralytic polio and of those with confirmed polio, 37 were either "worried well," did not meet the criteria for post-polio syndrome, or had a co-existing diagnosis that

TABLE 1. Status of All Patients Evaluated in the TIRR Post-Polio Clinic July 1984-June 1985

	No. of Persons
Total evaluated	174
No polio stigmata, normal EMG	5
Confirmed polio with new health problems	169
Worried well	4
Problems probably not polio-related	21
Problems probably polio-related but do not fulfill post-polio syndrome criteria*	12
Problems probably polio-related and fulfill post-polio syndrome criteria	132

*Each has only one new health problem; none has new atrophy.

TABLE 2. Non-Polio Medical Conditions Associated With New Health Problems in 21 Patients

Medical Condition	N	%
Respiratory disease	15	71
Obesity	2	10
Alcoholism	1	5
Disk disease	1	5
Cancer	1	5
Diabetes	1	5
Total	21	101

accounted for their new health problems. This leaves a total of 132 patients with new health problems *probably* related to their polio and with a presumptive diagnosis of post-polio syndrome.

Table 2 lists a frequency analysis of the non-polio medical conditions that were diagnosed to be the principal or only explanation of the patient's new health problems. Of these, respiratory disease was by far the most common, accounting for 15 or 71%. These patients were not included in any additional analyses of the post-polio group.

The remainder of the data concerns analyses of the 132 persons with a *presumptive* diagnosis of post-polio syndrome. Table 3 summarizes selected characteristics of this group. Approximately two thirds are women, 92% (122) identify themselves as white, and the median age is 45 years with a range from 24 to 86 years. While the majority of these patients (54%) are between the ages of 40 and 59, a sizeable group is under 40 (33%) and a somewhat smaller group (14%) over 59. The median number of years since polio is 38 and ranges from 24 to 85 years.

TABLE 3. Selected Characteristics of Post-Polio Syndrome Group (N = 132)

	N	%
Sex		
men	46	35
women	86	65
Totals	132	100
Race		
white	122	92
black	1	1
others	9	7
Totals	132	100
Current Age		
median	45 years	
range	24-86 years	
Duration of polio		
median	38 years	
range	24-85 years	

TABLE 4. Characteristics of Post-Polio Syndrome Group at Onset of Polio (N = 132)

	N	%
Hospitalized		
yes	108	82
no	22	17
unknown	2	1
Totals	132	100
Paralysis		
4 limbs	57	43
1 limb	26	20
Ventilator Use		
yes	21	16
no	111	84
Totals	132	100
Age		
median	7 years	
range	0-44 years	

The characteristics of the group with post-polio syndrome at onset of polio are shown in Table 4. The median age at onset was 7 years; 108 (82%) were hospitalized; and almost half (43%) had involvement of all 4 limbs. A somewhat smaller group of 21 (16%) required the use of a ventilator either part or full-time during the onset of polio.

The most common new health and activities of daily living (ADL) problems are listed in rank order in Table 5. Among the new health problems, fatigue was experienced most commonly (89%), followed by muscle pain (71%), joint pain (71%), and weakness in previously affected (69%) and unaffected (50%) muscles. The total number of persons experiencing muscle or joint pain was very high (113 or 86%) as was the total number of persons

TABLE 5. Most Common New Health and ADL Problems (N = 132)

	N	%
Health problems		
fatigue	117	89
muscle pain	93	71
joint pain	93	71
weakness:		
previously affected muscles	91	69
previously unaffected muscles	66	50
cold intolerance	38	29
atrophy	37	28
ADL problems		
walking	84	64
climbing stairs	80	61
dressing	23	17

who experienced weakness in previously affected or unaffected muscles (110 or 83%). By contrast, the percent of people experiencing cold intolerance (29%) and atrophy (28%) was considerably less. Among all 132 patients examined, none was experiencing new atrophy by itself. That is, nobody complained of atrophy as the only new health problem. The total number of persons experiencing one or more new difficulties with ADL was large (103 or 78%) with walking (64%) and climbing stairs (61%) experienced most commonly.

Table 6 shows a frequency distribution for the 6 most commonly experienced new health problems for all 132 persons with post-polio syndrome seen in the clinic. For purposes of this analysis, pain includes muscle and/or joint pain, weakness includes weakness of previously affected and/or unaffected muscles, and functional loss refers to any change in major areas such as walking, climbing stairs, or transfers. Among the 11 persons (8%) who had only 2 problems, the most common complaints were pain (7), weakness (4) and fatigue (4). The same pattern was seen in many of the other patients, with the most common cluster consisting of *fatigue, pain, weakness and functional loss*. Cold intolerance and atrophy were experienced most commonly along with a set of 4 or 5 other problems. As noted previously, none of the 132 patients with post-polio syndrome or the additional 12 with one new health problem were experiencing atrophy as the *only* new change in their health.

Table 7 compares selected characteristics between persons who experienced new atrophy and those who did not. Age at onset of polio, ventilator use, and hospital status at onset were very similar for the 2 groups treated. In contrast to patients who did not have new atrophy, those who did have it were divided almost equally between the sexes, had a larger number of limbs paralyzed at onset, and had a longer median time to onset of the first new health problem.

Although the group of patients with post-polio syndrome share much in

TABLE 6. Number of Problems and Frequency of Persons Experiencing Each New Problem for 6 Most Common Problem Areas (N = 132)

No. of Problems	No. of Persons (%)	New Health Problems*					
		F	P	W	FL	CI	A
2	11 (8%)	5	7	5	3	2	0
3	22 (17%)	18	16	15	11	1	2
4	51 (39%)	49	46	45	45	5	7
5	36 (27%)	33	32	33	32	18	16
6	12 (9%)	12	12	12	12	12	12
Totals	132 (100%)	117	113	110	103	38	37

*F = fatigue; P = pain in muscles and/or joints; W = weakness in previously affected and/or unaffected muscles; FL = functional loss in walking, climbing stairs, dressing, etc.; CI = cold intolerance; A = new atrophy

TABLE 7. Comparison of Patients With and Without New Atrophy

	Atrophy		No Atrophy	
	No.	%	No.	%
Sex				
male	16	45	30	32
female	21	55	65	68
Hospitalized at Onset*				
Yes	28	78	80	85
No	8	22	14	15
Ventilator at Onset				
yes	6	16	15	16
no	31	84	80	84
median age at onset	7 years		7 years	
median number of limbs paralyzed	3		2	
median time to first problem	35 years		31 years	

*Hospital status at onset unknown for 2 subjects

common, their experience with new health problems was not identical. More specifically, *the time to onset* for the first problem varied considerably among different subgroups of the larger population. However, because the duration of polio in this group ranges from 24 to 85 years, there was a large variation in the number of years respondents were at risk for developing new problems. To compensate for this large variation of time since onset, we used a modified life table technique to identify the patient characteristics present at onset of polio that were most commonly associated with developing new health problems later in life. The 4 variables at onset of polio that were strongly associated with developing new health problems many years later *at a shorter interval* were: required hospitalization (ν no hospitalization), experienced paralysis or paresis of all 4 limbs (ν only one limb), were 7 years or older at onset (ν under 7), and required a ventilator (ν no ventilator). The time to onset of new problems for men ν women, by contrast, was not significantly different, although the trend suggests women tended to have new problems somewhat earlier than men. When the experience of only women and men who were hospitalized is examined, however, this trend becomes statistically significant. Table 8 summarizes these 5 variables with respect to developing the first new problem and lists the median time and standard error from polio to onset of the problem and the level of significance between the subgroups using a generalized Savage (Mantel-Cox) test.

Table 9 lists the most common interventions and recommendations for patients seen in the clinic with post-polio syndrome. All patients were given at least one intervention and/or recommendation and most received two or more. For example, a large majority were given advice and/or a prescription regarding type and amount of exercise, weight loss, and level of activity. And

TABLE 8. Factors Associated with Developing New Health Problems and the Median Time Post-Polio to Onset of First New Problem (N = 132)

	N	Median Time* \pm SE	P
Hospitalized**			
yes	108	31 \pm 0.745 years	0.00001
no	22	40 \pm 1.0 years	
Paralysis			
4 limbs	26	28 \pm 1.0 years	0.0001
1 limb	57	34 \pm 1.6 years	
Age at onset			
<7	64	33 \pm 1.0 years	0.005
\geq 7	68	29 \pm 1.0 years	
Ventilator			
yes	21	28 \pm 2.3 years	0.0274
no	111	31 \pm 1.1 years	
Sex***			
male	46	33 \pm 1.3 years	NS
female	86	33 \pm 0.8 years	

*Median time and SE from onset of polio to occurrence of problem

**Data not available on 2 subjects

***For hospitalized patients only, women more likely to have new problems and at a shorter interval post-polio than men; $P < 0.007$

virtually everybody was counseled on the need to reduce stress in their lives—both physical and emotional. The most common prescriptions for durable products were written for new and/or modified aids to improve posture, diminish pain, and enhance comfort. These included corsets, lumbar rolls, neck pillows, wheelchair positioners, canes, and crutches, and were offered to 115 (87%) persons. Prescriptions for new and/or modified braces were provided to 69 (53%) patients, and for new and/or modified wheelchairs to 34 (26%) persons. The great majority (95%) of brace prescriptions were for lower limb orthotics and almost two thirds (15 or 63%) of the new wheelchair recommendations were for partial or full-time motorized chairs or 3-wheeled carts.

DISCUSSION

The data presented here describe a group of 132 consecutive patients with a presumptive diagnosis of post-polio syndrome who were identified from among all patients screened in an outpatient clinic during a 12-month period. All of these patients were evaluated by the same team using uniform, agreed upon assessment techniques in the post-polio clinic at The Institute for Rehabilitation and Research. The term post-polio syndrome is used intentionally in preference to other terms such as post-polio sequelae or the late effects of polio for two reasons: 1) it is gaining wider acceptance in usage among both

TABLE 9. Most Common Interventions and Recommendations

	N	%
Aids		
new	107	81
modified	8	6
Activity reduction		
yes	85	64
no	47	36
Exercise		
change type/amount	84	64
no change	9	7
Orthotics		
new	39	30
modified	30	23
Weight loss		
yes	68	52
no	64	48
Wheelchairs		
new	24	18
modified	10	8

medical and lay communities, and 2) it is developing sufficient specificity to be clinically useful. Although our understanding and definition of the syndrome will undoubtedly continue to evolve as we acquire additional knowledge, for the purposes of this study we have used the following 5 criteria to make a diagnosis of post-polio syndrome: 1) a confirmed history of paralytic polio; 2) partial to fairly complete neurologic functional recovery; 3) a period of neurologic and functional stability of at least 15 years duration; 4) the onset of 2 or more of the following health problems since achieving a period of stability: fatigue, muscle and/or joint pain, weakness, functional loss, cold intolerance, new atrophy; and 5) no other medical diagnosis to explain the new health problems.

In this group of patients, new atrophy was relatively uncommon (28%) so the term progressive post-polio muscular atrophy (PPMA) clearly is not appropriate for the majority of these patients. On the contrary, post-polio syndrome appears to be a more general classification under which PPMA is an important subtype. The hypothesis that PPMA is in fact a subtype of post-polio syndrome and not an altogether different entity is supported by 2 observations in this group of patients: 1) new atrophy did not occur in any of the subjects as the only new health problem, and 2) when it did occur, atrophy tended to be present when there were 4 or 5 other problems as well.

Although it is impossible to know how representative these patients are of the larger population of post-polio persons who are experiencing new problems, it is of interest to note how similar the characteristics and experiences of this group are compared to those reported in the earlier questionnaire studies

[1, 2]. For example, in both the clinic and questionnaire studies, two thirds of each group were women, the current median ages were in the mid-to-late 40s, and the median duration of polio was 38 or 34 years for the clinic and questionnaire groups, respectively. Both groups experienced fairly severe polio at onset with greater than 80% requiring hospitalization, over 40% having 4 limbs paralyzed, and approximately 20% requiring use of a ventilator. In addition, the 6 most common new health and ADL problems were the same in both groups. The interval from polio to onset of new problems was also very similar in the 2 studies ranging from 28 to 40 years, depending upon the problem. Finally, the factors at onset associated with earlier occurrence of new problems were the same: degree of severity and age.

The finding that there is considerable similarity in the characteristics and experiences of these 2 groups is reassuring as the questionnaire study had a number of methodologic limitations and the conclusions, which were widely published, could have been, unintentionally, quite misleading. By contrast, the present study was able to avoid many of the limitations inherent in a questionnaire approach. Specifically, we substituted self-report with a comprehensive, standardized evaluation to confirm the diagnosis of polio and the sequence and details of subsequent clinical events, and then obtained any necessary laboratory tests and outside consultations to rule out the presence of other medical diagnoses or conditions that might explain the subject's new health problems. Thus, we were able to exclude from analysis patients who would have been included in a questionnaire study.

This leaves for consideration a fairly large group of individuals who have a presumptive diagnosis of post-polio syndrome and about whom a considerable amount is known. Figure 1 summarizes some of this information in the form of the natural history of poliomyelitis for the clinic group. The median time of onset was 7 years (point A to B) and the median time to achieve full recovery was 8 years (B to C). The period of neurologic and functional stability in this group, lasted a median of 25 years (C to D), followed by the onset of new health problems (ie, showed gradual deterioration of neurologic and functional status) that had existed a median of 5 years before evaluation in the post-polio clinic (solid line from D to E). The dotted line represents the clinical course of polio survivors not seen in the clinic and who are presumably not experiencing new health problems related to their prior polio. In an earlier study, this group was estimated to represent three quarters of the polio population [3]. Although the long-term prognosis for the clinic group remains unknown (E to F), the preliminary follow-up over the course of one year suggests that most of these individuals are experiencing a slowly progressive but basically benign course. This relatively benign course is consistent with the observations reported by Dalakas et al [4] in a group of individuals who all had new atrophy and weakness and had been followed for a mean of 12.2 years.

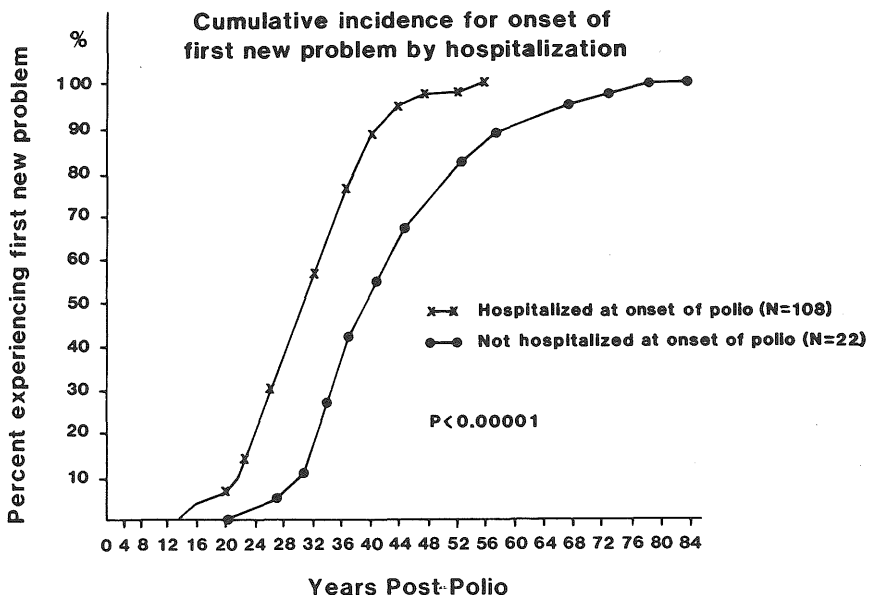


Fig. 2. The difference in experiences for onset of new problems for patients hospitalized and not hospitalized during the original polio illness.

new health problems by sex. Although sex was not significantly associated with developing any of the new health and ADL problems earlier, women had more problems and developed them slightly earlier post-polio than men. If, however, all persons who were not hospitalized are excluded and only the experience of the men and women who were hospitalized at onset is analyzed, then the difference becomes significant ($P > 0.007$); the median time from polio to onset of the first new health problem for women is 31 years and for men 35 years.

The treatment for persons with post-polio syndrome is conservative and relatively straightforward. Table 9 provides an overview of the interventions we used in this group of patients. However, a simple listing of the number of things prescribed or recommendations offered is deceptive. The fact is that post-polio patients often present with a series of complex interrelated problems that are diagnostically difficult to sort out and represent a formidable challenge to manage clinically. In the experience reported here, we wrote a large number of prescriptions but dispensed an even larger amount of education, advice, and counsel. Because many of the patients had become disenchanted or distrustful of the health care system from previous negative experiences, we found that it frequently took a number of clinic visits to establish enough trust so some of our recommendations would be tried. Thus,

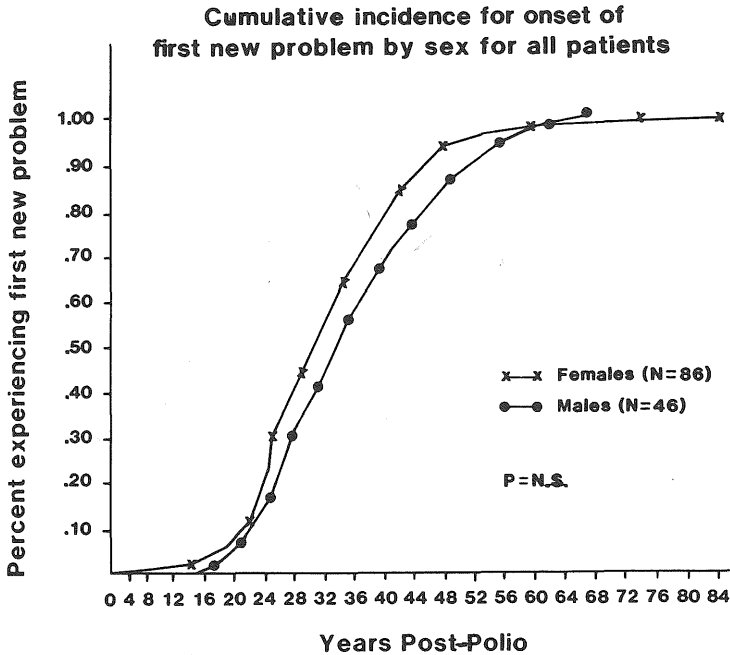


Fig. 3. The difference in experience for onset of new problems for men v women.

the number of interventions listed in Table 9 do not necessarily reflect the number of aids or those that were actually acquired or modified. Many patients were so accustomed to an old brace they had used for 20 or 30 years that they were unwilling to make a change even though it might improve their function or diminish their pain. However, among those patients who were willing to make changes and reduce their activity level, change their type of exercise, or go back to using a wheelchair part-time, we noticed several encouraging outcomes: 1) we were able to make them more comfortable and reduce their fatigue and pain; and 2) over a period of one year follow-up, we found that the progression of weakness was less and some people were beginning to stabilize their strength and occasionally improve it. Although the etiology of the post-polio syndrome remains obscure, we feel that these kinds of observations support the view that it is primarily an overuse phenomenon and, therefore, carries a good long-term prognosis.

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DISCUSSION

DR. BRADLEY: Do you have any data that actually looks across the whole body of people who had polio at different ages and then developed late onset problems?

DR. HALSTEAD: I think that what you are asking is, is there a break point at which age becomes more or less important? We have done an age at onset analysis on almost 1,000 people. It is interesting that data from the questionnaire and the clinical studies are very similar. When you pool all the data, it does in fact look like there is something of a linear relationship. In breaking it down into 5-year intervals, it was quite clear that patients, for example, who had onset of polio in the 5–9 year age group, have more problems and they occur sooner than the younger group in the 0–4 year interval. This is true up through 25–35 years of age. The interesting thing is that when you look at polio in general in terms of its severity, there is also a relation to age at onset that was well known by the epidemiologists reporting in the 40s and 50s. That is to say, people who were younger at onset tended to have milder polio and those who were older had more severe disease. It could be that age is a confounding variable and not an independent variable.

DR. DAUBE: What, in your clinical impression, is the basis for pain? Is this just because joints are being overused? Do you think there is muscle damage that is occurring?

DR. HALSTEAD: I would separate the joint pain from the muscle pain. I get the impression that the joints are hurting because of a wear and tear phenomenon. Yet, interestingly, when you get x rays, the radiologic picture of the joints shows much milder changes than you would expect based on the amount of pain or deformity. The muscle pain is a little harder to evaluate. I experience muscle pain myself and am daily trying to figure it out. At times, there seems to be a hypersensitivity quality to it, and at other times, it is deep and aching. Generally, it gets much better with rest and both types do better with mild analgesics and with heat. Other people describe different types of pain, and I am not sure there is a single basis for the muscle pain. I think there may be different types and people obviously experience them differently.

Late Sequelae of Paralytic Poliomyelitis in Olmsted County, Minnesota*

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INTRODUCTION

In 1984, data were presented by Codd et al [1] at the First Research Symposium on the Late Effects of Poliomyelitis concerning subjects in Rochester, Minnesota, who had previously experienced an episode of well-documented paralytic poliomyelitis. This group has subsequently been expanded to include all residents of Olmsted County, Minnesota, who had paralytic polio between 1935 and 1959. Two hundred eighty-six subjects were identified, and 276 have been located for follow-up. In our initial study, the patient's present status was ascertained by questionnaires administered both in written form and by telephone. Approximately 22% of respondents reported that they were having some type of difficulty. Although this proportion of the total group was lower than that reported from other surveys of polio survivor groups, the types of symptoms were similar. Of those reporting difficulty, 60% reported increased fatigue, 70% new weakness, 66% joint pain, and 46% to 50% muscle pain and cramping, respectively. These symptoms were usually related to exertion.

Several hypotheses have been proposed to account for this late deterioration:

- 1) A new loss of motor neurons either by accelerated attrition of overworked or previously injured neurons with age or by reactivation of polio virus.
- 2) A failure of nerve terminals within muscle because of overwork, failure to remodel, or because the aging neuron cannot maintain the large number of nerve terminals established during recovery from polio.

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- 3) New inflammatory disease of muscle or new and separate disease of peripheral nerve.
- 4) Cumulative effects of aging and systemic diseases associated with aging (diabetes, cancer, heart disease, obesity) causing accelerated debility in the person with the residual of polio.
- 5) Muscle and joint pain caused by prolonged use of muscles working around and across joints with suboptimal mechanical properties. This might include prolonged weight bearing on marginally stable joints, actual joint deformities such as scoliosis and degenerative arthritis, and unusual mechanics imposed by tendon transfer.
- 6) Psychologic factors.

To determine both the nature and extent of this problem in this unique population-based sample of patients, a detailed clinical trial has been initiated. Ultimately, all subjects will be examined once and then reexamined 4 years later. It is essential to examine the population at least twice in order to establish objective assessments of deteriorating function.

In this communication, the pilot data from 31 subjects who have completed the first examination will be presented.

METHODS

Selection of Subjects

The centralized diagnostic index at the Mayo Clinic provides a unique opportunity to conduct population-based research. Since the early part of this century, residents of Rochester and Olmsted County, Minnesota, have received their medical care primarily at Mayo and its affiliated hospitals. Diagnoses have been indexed and processed for automated retrieval. Diagnoses of Olmsted County residents receiving medical care at other institutions or practices in Olmsted and surrounding counties are also linked for retrieval within the same system.

Diagnostic criteria for paralytic poliomyelitis included all of the following: 1) a medical history compatible with poliomyelitis; 2) fever; 3) stiff neck and or stiff back; 4) 10 to 500 cells per cc of spinal fluid taken during the acute or early convalescent period of the disease; 5) spinal fluid protein elevated above normal limits; 6) demonstrable muscle weakness or paralysis that had been detected and had persisted during at least 2 examinations carried out at an interval of at least several hours. (National Conference on Recommended Practices for the Control of Poliomyelitis, Ann Arbor, Michigan, June 1949)

All persons in the population who contracted polio between the years 1935 and 1959 were identified from the centralized records-linkage system. This time period encompassed the principal epidemic years in that area: 1946,

TABLE 1. Characteristics of all Patients with Paralytic Poliomyelitis in Rochester and Olmsted County, Minnesota, between 1935 and 1959

	Rochester and Olmsted County Total
Total Cases	286
Deaths in the acute phase	30
Deaths in subsequent years	23
Untraced	10
Age range at time of polio	2 months to 59 years
Median age	9 years
Sex ratio (F:M)	1:1

1949, and 1952. There were 286 cases of paralytic polio in the 24-year period, with just over 50% occurring in 1952 (Table 1). Thirty people (10.5%) died in the acute phase of the illness, and 23 died in later years. The remaining 233 formed the cohort for follow-up. Two hundred twenty-three have been located, and efforts continue to locate the remaining 10 subjects. It should be mentioned that in the same time period, there were approximately 150 cases of nonparalytic polio and 170 cases of suspected polio. Follow-up has not been extended to include these cases.

For the initial clinical study, we selected those survivors from the original cohort who currently reside in Rochester and the surrounding area. We also randomly selected an equal number from those who were complaining of deterioration and those who were not. This intentionally biases the study toward those with difficulty. After 50 patients have been studied once, the methodology will be reevaluated to determine whether it is appropriate, and then the study will be extended to the whole group so that this initial bias will be lost if all subjects are entered.

Eligibility

All selected patients were initially interviewed by one of two neurologists (AJW or WJL). The purpose of this interview was to confirm eligibility from both the record and the patient's memory. They were required to have had paralytic polio and to have lived at that time within Olmsted County, Minnesota. The study was then explained in detail and informed consent obtained. No attempt was made to elicit complaints, and patients were cautioned against volunteering present symptoms.

Neurologic Disability Score

The patient was then examined by the neurologist, who performed manual muscle strength testing of defined muscles (Table 2). The examiner compared the observed muscle strength with an experiential norm for a person

TABLE 2. Panel of Muscles Used in the Polio Disability Score*

NAME _____ MC # _____ DATE _____

AGE _____ SEX _____ EVALUATION # _____

Scoring: Strength 0 = no deficit; 1 = mild weakness; 2 = moderate weakness; 3 = severe weakness; 4 = no movement.

Muscle	Strength
Facial muscles	/
Masseter	/
Genioglossus	/
Neck Extensors	/
Neck Flexors	/
Supraspinatus	/
Infraspinatus	/
Deltoid	/
Biceps	/
Triceps	/
Brachioradialis	/
Wrist Flexion	/
Wrist Extension	/
Finger Flexion	/
Finger Extension	/
Thenar	/
Interossei	/
Abdominal	/
Iliopsoas	/
Quadriceps Femoris	/
Ext/Int Hamstring	/
Anterior Tibial	/
Peroneus Longus	/
Ext. Dig. Longus	/
Flexor Dig. Longus	/
Posterior Tibial	/
Gastrocnemius	/

*This is part of a comprehensive protocol examination performed on each patient. Grading of muscle bulk, fasciculations, reflexes, sensation, gait, scoliosis, and speech were made but are not presented in the data of this pilot study.

of comparable age, build, and physical activity. The grade assigned to each muscle (0 is normal strength, 1 is 25% loss of strength, 2 is 50% loss of strength, 3 is 75% loss of strength, and 4 is 100% loss of strength) is a linear progression that expresses observed strength as a function of normal. This differs from the MRC grading scale in which numbers are assigned in a nonlinear fashion to defined attributes of muscle function. The former approach has the advantage that numbers can be handled additively for statistical analysis.

Questionnaire

Each patient then completed a questionnaire composed of 337 items inquiring about limb and bulbar weakness (Table 3) and activities of daily living (Table 4). The questionnaire given to the polio group is also being administered in modified form to a group of age-matched normal controls from the same population base.

For data analysis, certain key items were extracted from this questionnaire to devise a progression score. For example, "The arm weakness has worsened since maximal recovery (X)Y ()N" would gain one point (Table 3) or "I could/can feed myself—independently and with ease (at maximal recovery) and only by using adaptive equipment (now)" would gain one point. The progression score would yield a maximum of 50 points for patients who felt they were deteriorating in every aspect of their function (Table 5).

Minnesota Multiphasic Personality Inventory (MMPI)

This standard questionnaire was administered to all subjects and scored in a standard fashion against normative data available in our institution.

TABLE 3. Upper Limb Strength*

Do you have <i>weakness in the arms or hands</i> ?	Y()	N()
If Yes, please answer the following statements or questions		
If No, go to the next section.		
The arm weakness is		
Present in one arm only	Y()	N()
Present in both arms	Y()	N()
About the same in both arms	Y()	N()
Much greater in one arm than in the other	Y()	N()
Mainly in the shoulder(s) and upper arm(s)	Y()	N()
Mainly at the wrist(s) and hand(s)	Y()	N()
I have difficulty raising my arms above my head	Y()	N()
I have trouble taking off a sweater	Y()	N()
I have difficulty opening jars and bottles	Y()	N()
I have difficulty turning keys	Y()	N()
The arm weakness has:		
Stayed the same since maximal recovery	Y()	N()
Worsened since maximal recovery	Y()	N()
If worsened, the deterioration:		
Occurred suddenly	Y()	N()
Took place gradually	Y()	N()
Occurred/began _____ year(s) ago (19_____)	Y()	N()

*An excerpt from the 337 item questionnaire.

TABLE 4. Activities of Daily Living*

<i>MOBILITY/DAILY ACTIVITIES</i>		
We would like you to assess your ability, both at your maximal recovery level and now, to get about and to manage a series of day-to-day activities. Please check just one of the three possible answers to each question.		
	At Maximal Recovery	Now
I could/can walk on a level surface		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()
I could/can manage a small flight of stairs (about 10 steps)		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()
I could/can get in and out of bed		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()
I could/can sit down/get up from a chair		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()
I could/can bathe or shower		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()
I could/can use the bathroom		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()
I could/can dress and groom myself		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()
I could/can feed myself		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()
I could/can carry out home activities (cooking, laundry, cleaning, etc)		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()
I could/can go shopping		
Independently and with ease	()	()
Only by using adaptive equipment	()	()
Completely unable to do this	()	()

*Excerpt from questionnaire.

TABLE 5. Items Contributing to the Progression Score Derived from the Questionnaire

Items	Progression Score
Fatigue	1
Pain	1
Progressive bulbar weakness	6
Progressive respiratory weakness	4
Progressive lower limb weakness	4
Progressive upper limb weakness	4
Functional capacity	10
Assistive devices	7
ADL or home modification	13
Total possible	50

Electrophysiology

Nerve conduction studies were performed in all 4 limbs on each patient and included median and peroneal motor, median, and sural sensory nerves bilaterally. The amplitudes of the evoked responses, distal latencies, F-wave latencies, and conduction velocities were measured for each nerve at standard distances and temperatures. Repetitive stimulation at slow rates was performed on each motor nerve. For each nerve, the number of motor units in the muscle was estimated using the method of motor unit counting of McComas [2]. Needle electromyographic examination was performed in 2 muscles in each limb. The extensor digitorum brevis and thenar muscles were examined bilaterally in all patients. In addition, the clinician who examined the patient neurologically selected a weak proximal muscle in each limb, which was also tested. These muscles were all tested in multiple sites for both spontaneous activity and voluntary motor unit potentials. The number of fibrillation potentials and fasciculation potentials were graded numerically. Motor unit potentials were assessed individually for amplitude, duration, number of phase reversals, and stability. Each of these was graded numerically as well.

Pulmonary Function Tests

Measurements of respiratory muscle function were made in the Mayo Clinic Pulmonary Function Laboratory. In this laboratory, absolute values are reported, and comparisons with normals by age and surface area were derived.

In this study, the following parameters were measured: height, weight, surface area, vital capacity, expiratory reserve volume, forced vital capacity (FVC), forced expiratory flow 25% to 50%, maximal forced expiratory flow, forced expiratory flow at 50% VC, maximal voluntary ventilation, maximal inspiratory (P_I max), and maximal expiratory pressure (P_E max). All of these, except for the last 2, are functions of the intrinsic properties of the lungs and

airways as well as of muscle. The last two (P_E max and P_I max) are functions only of muscle strength since there is no airflow.

Isometric Strength Measurement

In order to complement the manual muscle strength testing, force generated isometrically across different joints was quantified in the Mayo Clinic Biomechanics Laboratory. The following actions were studied bilaterally: knee flexion, knee extension, ankle plantar flexion, ankle dorsiflexion, elbow flexion, elbow extension, forearm pronation, forearm supination, and grip strength. The isometric mode was utilized in order to minimize contributions from joint mobility and coordinative function. Measurements were reported in both absolute force units and as percentages compared with normals matched for age, weight, sex, build, and dominant/nondominant side.

Functional Tests

A battery of standardized functional tests was carried out in the Department of Occupational Therapy. These results were also reported in both absolute numbers and as percentiles of a population matched for age, sex, and level of manual skill expected in their occupation. These tests included standard measurements of upper arm girth, thigh girth, and calf girth; time to walk 100 feet; the Minnesota Rate of Manipulation; and the Crawford Small Parts Dexterity Test.

Data from the Old Record

In all cases, the contemporaneous record of the acute illness was available. This included history and clinical observations made at the time, and results of cerebrospinal fluid (CSF) examination. There was also a protocol neurologic examination recorded on the Mayo Clinic Neurologic Examination Record. This has been in continuous use, with minor modifications, for 60 years. The muscles tested are examined in a standardized manner [3], and the grading system in use between 1935 and 1959 was identical to that used and described above. This record yielded a contemporaneous validation of the illness and a neurologic disability score at the time of maximal deficit (NDS max) derived from examination of the same muscles as used in this protocol (Table 2).

After all of the examinations were completed, the patient returned to the neurologist. The questionnaire was checked for completeness and patient understanding, and further areas of difficulty were explored in an open question and answer format. The results were discussed with individual patients to encourage follow-up. An extremely high patient satisfaction rate was noted.

RESULTS

Selected parts of the study are presented at this time; the remainder of the data will be presented at the completion of the first examination of all patients, and after the second examination of all patients 4 years later. At this time, 31 patients have completed the study. Ten individuals reported no difficulties of any kind, 2 reported fatigue as their only symptom, and 2 reported pain as their only symptom. Seventeen reported new, perceived, specific limb weakness. This last group may also have reported pain and fatigue as additional symptoms. The types of complaints are summarized in Table 6. Of note, the maximum progression score reported by any individual was 8 (out of a possible 50), and only 2 patients reported change in their functional capacity or required new modification of their home (eg, installation of bath rails). None required new assistive devices and none reported increased respiratory difficulty.

In this group of patients, the following variables were compared with progression score: age at onset of polio, present age, interval since polio, severity of polio at onset (NDS max), severity of present disability (NDS), creatine kinase (CK) level, CSF cell count at time of disease, and CSF protein level at time of disease. None of these variables showed a significant association; CK ($R^2 = 0.4$) and interval ($R^2 = 0.3$) showed a trend toward association, which may be significant as larger numbers are attained.

The electrophysiology for index data demonstrated abnormalities of size and recruitment of motor unit potentials that showed the original disease to have been much more widespread than had been clinically evident. In a given muscle, amplitude of the compound muscle action potential (CMAP), motor unit potential (MUP) count, and fibrillation potentials corresponded to the severity of clinical involvement of that muscle. However, if limbs reported as progressing were matched for limbs of equal weakness without reported regression, there was no difference in amplitude of CMAP, conduction velocity, distal latency, F-wave latency, MUP count, recruitment, or with

TABLE 6. Patients Complaining of Difficulty Within a Given Area of the Progression Score

Items	Number of Patients Reporting
Fatigue	11
Pain	13
Progressive bulbar weakness	1
Progressive respiratory weakness	0
Progressive lower limb weakness	13
Progressive upper limb weakness	8
Functional capacity	2
Assistive devices (braces, crutches, etc)	0
ADL/home modification (handrails, elevators, etc)	1

those attributes associated with ongoing denervation (fibrillation potentials and MUP variability). Therefore, although the electrophysiologic findings correlated with the severity of limb involvement, they were unable to predict the likelihood of reported progression in a given limb or muscle. Electrophysiology allowed a quantitative approach to following individuals. It also provided information about additional unrelated disease in 2 patients (one with carpal tunnel, the other with diabetes and a generalized peripheral neuropathy).

The major observation of note concerned the likelihood of reporting difficulty in a weakened limb. If individuals were divided into 5 sites (bulbar, right and left upper, and right and left lower limbs), a total of 155 sites were examined. Of these, 33 or 21% were reported as progressing. If the sites were partitioned according to severity of original weakness, 45 sites with NDS max ≥ 8 were observed. Of these, 56% were reported as progressing. However, only 8/110 (7%) with NDS max < 8 were reported as progressing (Table 7). If the results are further partitioned according to upper and lower limbs, then of 62 legs examined, 22 had NDS max ≥ 8 and of these 18 (82%) were reported as progressing. Of 62 arms examined, 18 had NDS max ≥ 8 , and 7 or 39% were progressing. Five of 31 bulbar muscle groups had NDS ≥ 8 and none reported progression. Therefore, progression is most likely to be reported in lower limbs that were most affected during the acute illness.

CONCLUSION

In this preliminary report, we have selected patients from a population-based group of subjects who had paralytic poliomyelitis while living in

TABLE 7. Progression Reported in Individual Limbs Separated According to Severity of Original Involvement in That Limb (NDS max)

Total sites examined (arms, legs, and bulbar)	155
Sites with reported progression	33 (21%)
Sites examined with NDS ≥ 8	45
Sites with reported progression	25 (56%)
Sites examined with NDS < 8	110
Sites with reported progression	8 (7%)
Total legs examined	62
Number of legs with NDS ≥ 8	22 (mean NDS 19.1)
Legs with reported progression	18 (82%)
Total arms examined	62
Number of arms with NDS ≥ 8	18 (mean NDS 17.6)
Arms with reported progression	7 (39%)
Total bulbar muscles examined	31
Number with NDS ≥ 8	5
Number with reported progression	0

Rochester or Olmsted County, Minnesota, between the years 1935 and 1959. The first phase of the clinical study involved detailed clinical and electrophysiologic examination of 31 subjects. These 31 patients were drawn from a population in which 22% had complained of difficulty. The group of 31 represented 14 subjects who had reported difficulty (45%) and 17 who had not. The first study [1] had been completed in 1984. In the present study, 21/31 (68%) complained of difficulty. This shift from 45% to 68% is thought to be due to 3 factors: 1) subjects are experiencing more difficulty with the passage of time; 2) there is a heightened awareness of the late effects of polio due to our interest in this population; and 3) the present questionnaire is much more detailed and, therefore, elicits more complaints.

Fifty-five percent of the patients report progression of weakness as a major symptom. However, it must be stressed that this relies on self-reporting. Pain and loss of joint function may be reported as weakness. The only way to document true muscle weakness is to carry out serial observations.

The major negative findings were that age and interval since polio were not major factors in determining the likelihood of difficulty. Electrophysiology did not predict progression when limb weakness was matched between those reporting progression and those not reporting progression.

The major positive conclusion was that subjects are much more likely to report progressive difficulty in a lower limb and in limbs that were most affected by the original disease. This does not exclude or support any hypothesis. However, it suggests strongly that overuse, rather than reactivation of disease, is a major factor in the progression of polio. This may involve both overuse of muscles and increased weight-bearing strain on lower limb muscles.

The etiology of the late effects of polio is probably multifactorial and will only be determined by sequential studies.

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DISCUSSION

DR. DALAKAS: Did you do the EMG studies blindly in unselected limbs without knowing whether or not the patient has new weakness?

DR. DAUBE: A total of 8 muscles were examined in each patient. When you do that and you do not know whether there is progression, obviously you have the risk that you will examine only muscles that are not progressing. But in fact, with that broad a sampling, you do get muscles that the patient subsequently reports are progressing. So what we have is a group of muscles that are nonprogressing, and those that are progressing in which we can then make the comparison. That was the purpose for selecting it that way and doing it blindly. I think you have to do that in order to determine whether or not the EMG has significance because we know you find changes in all the muscles and unless you make a comparison blindly, you cannot make the assessment.

DR. BRADLEY: What is the relationship between MMPI and the pain? You must have the information already since you have gotten a group that had no complaints and a group that had complaints.

DR. WINDEBANK: The MMPI in our Rochester group of patients, apart from the one who had inpatient hospitalization for psychiatric illness, were completely normal. In our Rochester group there is *no* relationship between MMPI scores and symptomatology.

DR. BROSTOFF: Could I ask about some associated symptoms that I see in the acute post-viral syndrome patients, that is, patients who have presumably infectious mono or an acute flu and have a relatively quick onset and no recovery from symptoms that are virtually identical to your post-polio patients? In addition to the symptoms outlined by Dr. Halstead, which are identical to the group that I see (and we must have 400 to 500 now), I ask for migraine and it may be classic migraine or headache described as an uncomfortable feeling in the head, arthralgia, which is morning pain and stiffness that tends to get better during the day, and also irritable bowel syndrome, that is, wind, bloating, and alteration of bowel habit. And in the groups of patients that I get, they can be referred by either the rheumatologist or the neurologist or the gastroenterologist for those presenting symptoms, but then are clearly shown to have, in my view, a post-viral syndrome with those as part of the picture.

DR. WINDEBANK: I think it is a very big area for discussion. Certainly we do ask about arthralgias. We do not ask about migraine or irritable bowel. However, all that information is available from the Mayo Clinic records if we wanted to go back and look for it.

Occurrence of Post-Polio Sequelae in an Epidemic Population

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INTRODUCTION

In 1977, a health survey by the National Center for Health Statistics estimated the number of persons with paralysis in a household and the etiology of the paralysis. Much to everyone's surprise, the number two cause of existing paralysis in America (second only to stroke), was polio, with 254,000 people suffering from polio residuals. Because many people who have had polio tend not to think of themselves as paralyzed unless they have lost the majority of function and strength of a limb, the actual number of individuals with post-polio weakness may number in the range of 400,000. Most of these persons showed improvement in strength and function for the first 10 years or so after onset, and then achieved a period of stability. They have completed higher education, married, raised families, and most have been employed full time.

Reports of isolated cases of "late progression of polio" have appeared in the medical literature since the late 1800s. Many of these have described a symptom complex resembling amyotrophic lateral sclerosis with progressive weakness, atrophy, and fasciculations. However, even the larger series of case reviews over many years implied that the problem of decreased strength and function years after polio was rare.

In the late 1970s, a former polio patient wrote a letter to the *Rehabilitation Gazette*, a newsletter for disabled people, about increased weakness and fatigue that he was suffering. As more and more people communicated similar experiences, the extent of these new problems began to be realized. By the 1980s, the popular press was speaking of "the return of polio" and "polio revisited." Medical practitioners and physical therapists found themselves confronted with a bewildering array of new problems suffered by people who once had polio and had enjoyed many years of stable function.

Commonly noted problems collectively described as "post-polio syn-

dromes" or "post-polio sequelae," included increasing weakness affecting new areas as well as those previously affected by polio, decreased endurance, muscle and joint pain, muscle atrophy, new or more severe breathing and swallowing difficulties, increased fatigue, loss of previously achieved function, and need for increased aids. Because of the fear that this phenomenon might resemble amyotrophic lateral sclerosis in its course and prognosis, it became apparent that the incidence and scope of the problem needed to be determined.

In 1983 and 1984, Halstead distributed questionnaires to over 500 members of community post-polio interest and support groups [1]. Two hundred and one respondents provided the first important data from a large group. The majority of these respondents were women (70%), who noted the onset of problems at approximately 30 years after the onset of polio. Over 50% had contracted polio after 1949.

Of this group, over 70% reported weakness, 87% complained of increasing fatigue, 75% had new muscle pain, and 41% experienced new breathing difficulties. This study and others by Halstead et al [1-4] of individuals coming to post-polio meetings and clinics confirmed these findings, and suggested that women, those who contracted polio at an age greater than 10 years, and those who had had very severe initial disease were the most likely to suffer from the new problems. Other smaller studies also found that the interval between acute polio and the onset of new problems was approximately 30 years.

To gain more objective data, and avoid selecting a self-referred symptomatic population, the Mayo Clinic examined a population closely documented in Olmsted County, Minnesota [5]. The investigators were able to review all recorded polio cases in the county from 1935 to 1955 and located a significant number of survivors. Out of 128 respondents to the questionnaire, 22% reported new problems or deterioration in function. Of those, 71% had new muscle weakness, 59% reported increased fatigue, 48% had muscle pain, and 25% found functional skills decreasing. This population was young at onset of polio and had more severe initial disease than the nonsymptomatic group. Because of the large span of years over which the polio occurred, there were some confounding variables, including susceptibility of the various age groups to polio over the 20-year period, differences in treatment, and the general effects of aging.

As a result, it was important to sample a group who was not self-referred to an interest group or clinic, who had polio within a defined period of time, and who had a reliable diagnosis and relatively uniform treatment. In 1952, 56,000 cases of polio occurred in the United States; this epidemic was Minnesota's largest (6,000 cases of paralytic polio) and was also prominent in the populations surveyed by both Halstead et al [1-4] and Codd et al [5]. We

located as many patients as possible who had been hospitalized in 1952–1953 at several Minneapolis hospitals (all of which had old patient records available for confirmation), to determine the occurrence and types of problems in this epidemic group. Most of the patients in this epidemic group had been treated by the Kenny methods.

Obviously, the population is selected for the need for hospitalization; thus, generalization of findings cannot be made accurately to the population of persons who had nonparalytic polio or who were not hospitalized. However, it must be realized that the descriptor “nonparalytic polio” was sometimes given to persons who were initially weak and appeared to rapidly recover “normal” function, whether or not they were hospitalized. Other factors, such as hospital bed availability, and consent of the family to hospitalize a member (often far from home) were other confounding variables. Thus, lack of hospitalization for an individual did not necessarily reflect severity of the initial disease. Also, the demands of an epidemic illness on limited health care resources often determined which patients were hospitalized, placed on ventilation support, or even had tracheostomies. Lastly, the young age of many individuals when they contracted polio contributed to hazy, often frightening memories; accuracy of reporting of acute events or degree of involvement is reduced by the effects of secondhand (parental or sib) information. Hopefully, the latter can be reduced by painstaking review of the old records for clarification of initial disease severity and status at acute rehabilitation discharge.

METHODS

Between July 1, 1952 and June 30, 1953, 1,619 patients were hospitalized at Sister Kenny Institute, Sheltering Arms Hospital, and the University of Minnesota hospitals in Minneapolis, Minnesota. None of these hospitals limited admissions by age of the patient. An estimated death rate of 4.8% from the Minnesota Department of Health left a projected 1,542 survivors to be traced. With the dedicated help of volunteers, the present addresses of 670 persons in that group, or 43%, were located.

This group was sent a 30-item questionnaire assessing the following: sex, date of birth, present age, date of onset of polio, education and employment history, dates and location of hospitalization, need for aids and degree of function for upper and lower limbs at discharge from acute polio rehabilitation and at present, breathing and swallowing problems in 1952 to 1953 and at present, and the presence of new problems, including increased weakness in old polio-affected areas and in new, previously unaffected areas, level of endurance, loss of functional activities, and presence of pain or cramping. A cover letter was sent, urging people to reply even if they did not note

deterioration so that a more accurate estimate of problems could be obtained.

Upon receipt of the questionnaires, the information was coded and entered into a Revelation data base on an IBM PC-AT computer for storage and retrieval.

DATA ANALYSIS

In addition to reporting response percentages to each question, chi-square contingency tables were done to test for independence between reported incidence of problems, age of onset, sex and other variables as well as the relationship between the variables themselves. Two-by-two chi-square tables are the best statistics to examine the proportions of individuals in the various categories. The hypothesis of independence was rejected at the 5% level of significance, with one degree of freedom and chi-square equaling 3.84, and at the 10% level at chi-square equaling 2.79.

RESULTS

Forty-nine percent of the questionnaires ($n = 327$) were returned, representing 21% of the original epidemic population pool in question. Characteristics of the prospective pool and of the respondents were compared and were not significantly different as to sex distribution or age at onset. The proportion of males to females corresponds more closely to the actual incidence of polio, particularly in the younger age group. There was no female bias in the respondents; the high response rate from females was testament to the perseverance of the volunteers in tracking down females who had married after leaving acute treatment and might be more difficult to trace. Thus, concerning age of onset and sex distribution, the respondents to the questionnaire fairly represent this pool of patients hospitalized for polio rehabilitation in Minneapolis, in 1952 to 1953. These figures are noted in Table 1.

The majority of these respondents still live in Minnesota, and a large

TABLE 1. Characteristics of Prospective Pool of Respondents

	Study Pool 6/52-7/53	Respondents to Questionnaire
Total	1,619	327
No. deaths	77	—
Death rate	4.8%	—
No. survivors	1,542	—
% Males	53%	57
% Females	46%	43
Mean age at onset	13	13

TABLE 2. Demographics

	%
Current residence	
Minneapolis-St. Paul	12
Other Minnesota	66
Neighboring states	7
Other USA	15
Education	
High school graduation	62
One or more years of college	29
Employment	
Employed since polio	92
males	97
females	84
Mean age of employed	46.4 years
range	34–79 years

number of them have completed higher education and have been employed (Table 2). This was a young population originally affected by polio, with the median age at onset 10 years, and a total of 76% under 19 years at onset. (Table 3). The present median age of respondents is 44 (mean of 47, range 34–79 years). Over one-half of this group were not using any ambulatory aids upon acute discharge in 1952–1953; 34 years later, over three-quarters do not use braces, canes, crutches, Kenny sticks, or wheelchairs. No group is reporting increased need for aids. The prevalence of upper limb involvement is low (Table 4). None of the patients is receiving ventilatory support at present.

New problems were reported by 41% of those questioned. Pain or cramping was the most frequently mentioned problem at 47%, followed by worse endurance (42%), and increased weakness (40%) (Table 5). The frequencies of new breathing and new swallowing problems were 11% and 13%, respectively.

TABLE 3. Age Distribution in Respondent Population

Age at Onset (yrs)	No.	% of Total
0–9	160	49
10–19	87	27
20–29	50	15
30–39	23	7
40–49	7	2

Median age at onset = 10.0 years

Mean age at onset = 13.0 years

Mode = 5.0 years

Range: 0–45 years

TABLE 4. Upper & Lower Limb Deficits

Ambulatory Status	1952-53* %	1986 %
No ambulatory aids	58	76
Cane(s), crutch(es), or Kenny stick(s)	26	6
Wheelchair use	5	5
Lower limb brace(s)	12	6
Upper Limb Involvement		
Upper limb weakness	4.5	3.9
Upper and lower limb weakness	1.5	0.6

*Discharge from acute polio rehabilitation

There was no correlation between age of onset and several of the new problems, with the exception that those who contracted polio between the ages of 20 and 29 had a significantly higher incidence of increased weakness, endurance, and breathing problems than younger groups. These data were examined both by 5 and 10 year groupings. A slightly younger age group (10 to 19) and slightly older (30 to 39) group reported a higher than expected frequency of swallowing problems than the very young group (0 to 9 years). As expected, the study group who had polio during this epidemic and were less than 10 years of age at onset do not appear to have a significantly higher risk of new problems (Tables 5 and 6).

As shown in Table 7, most of the people reporting increased weakness tended to localize this to areas previously affected by polio. Only a small percent (16%) felt they were weak in previously unaffected areas only; one third of the subjects felt that both old and new areas were affected or had trouble defining areas of weakness as old or new.

There was no significant relationship of fatigue, pain, breathing, swallowing difficulties, or new weakness to sex, with the exception of a small subgroup of patients who were female and very young (0 to 5 years) at onset. These patients appeared to have a slightly higher incidence of weakness in

TABLE 5. Age at Onset and Percent Reporting New Problems

Age at Onset	Problems in Last 10 Yrs. %	Increased Weakness %	Pain or Cramping %
0-9	39	36	46
10-19	37	37	45
20-29	52	58*	54
30-39	43	39	48
40-49	71	57	43
All ages	41	40	47

*Worse compared to age groups 0-9, 10-19, at $P \leq 0.05$

TABLE 6. Age at Onset and Percent Reporting New Problems

Age at Onset	Worse Endurance %	Breathing Problems %	Choking Problems %
0-9	36	10	6
10-19	44	13	16*
20-29	58*	22*	14
30-39	39	17	30*
40-49	29	14	0
All ages	42	13	11

*Worse compared to age groups 0-9, at $P \leq 0.05$

previously "unaffected" areas only when compared to males ($P < 0.10$). There were no significant differences between sexes as to prevalence of increased weakness overall or increased weakness in previously affected areas in any age group.

Severity of illness does appear to play a role in predicting incidence of new problems, though not to the degree seen in previous studies. Compared to Halstead's studies, our proportion of severely affected respondents was small. Lower limb weakness of a severity requiring aids for ambulation was the only historical fact associated with future increased weakness. This history of lower limb weakness requiring aids in 1952 to 1953 accompanied by a history of bulbar and/or breathing problems, also predicted a significantly increased risk of breathing and swallowing problems at present (Table 8).

Surprisingly, a smoking history does not increase the reporting of breathing problems or any other new problems, but does increase the likelihood of decreased endurance (Table 9).

Thus, a somewhat older group (older than 10 years at onset) with significant lower limb weakness in 1952 to 1953 appear to be at most risk for

TABLE 7. Frequency of New Problems in Males and Females

Problem	Total %	Males %	Females %
Pain or cramping	47 (154)	44 (82)	51 (72)
Decreased endurance	42 (136)	41 (76)	43 (60)
Increased weakness*	40 (132)	37 (70)	46 (64)
new weakness in previously "unaffected" areas†	16 (22)	17 (12)	15 (10)
new weakness in old polio areas only†	51 (70)	59 (42)	43 (28)
Breathing problems	13 (43)	14 (26)	12 (17)
Swallowing problems	11 (37)	12 (22)	11 (15)

*Increased weakness includes those describing weakness in new and old areas as well as those uncertain as to areas previously affected by polio

†Percent of those describing "increased weakness"

() = number

TABLE 8. Severity of Polio at Onset and Frequency of New Problems

New Problems	Used Lower Limb Aids %	Used Wheelchair Only %	Breathing Problems in 1952-53 %	Breathing Problems and Lower Limb Aids in 1952-53 %
New problems (overall)	47	50	53	70
Increased weakness	48*	56	47	70
Pain or cramping	46	50	68†	70
Worse endurance	43	62	53	70
Breathing problems	18†	19	74*	70*
Choking problems	10	12	37*	40*
(n)	(127)	(16)	(19)	(10)

*Significant at $P < 0.05$ †Significant at $P < 0.10$

developing new problems. There does not appear to be an association between sex or history of breathing difficulties and most of the newly reported problems.

DISCUSSION

As opposed to other studies, there was neither sex bias in reporting nor any clear-cut association of new problems with sex. Weinstein [6] did find that females younger than 15 years were more likely to have quadriplegia from acute polio than those 15 and older; spinal paralytic polio was distributed evenly across all age groups in Weinstein's 1957 analysis of patients in Boston. This might account for increased weakness in our group of females younger than 5 years, but would not explain why the significant difference would be restricted to weakness in newly affected areas only. Certainly, examination of a larger population may clarify this. With both sexes, severity of disease did play a role in predicting new problems, as seen by Halstead et al and Codd et al [1-5]; this was noted despite the fact that our group was not as severely

TABLE 9. Smoking Status and Frequency of New Problems

New Problem	Total %	Smokers %	Nonsmokers %
Pain or cramping	47 (154)	52 (36)	48 (117)
Decreased endurance	42 (136)	52 (36)*	39 (96)
Increased weakness	40 (132)	47 (33)	40 (99)
Breathing problems	13 (43)	18 (13)	12 (29)
Swallowing problems	11 (37)	17 (12)	9 (24)

*Significant at $P < 0.10$

() = number

affected as their patients (ie, none on ventilators, etc). It should be noted that in their studies of patients with post-polio spinal muscular atrophy (patients with weakness, atrophy, and fasciculations resembling the symptoms of ALS), Dalakas et al [7, 8] did not report an association of sex, age of onset, or initial severity of disease with new symptoms.

In contrast to the reports by Halstead et al, most people in our study had improved function, with a greater proportion ambulating without aids 34 years after onset. The percentage of wheelchair users remained stable. The relatively low number of those using lower limb bracing in 1952 and 1953 and at present may also reflect the fact that this group of patients was rehabilitated in facilities greatly influenced by Sister Kenny herself. The Sister's aversion to bracing, especially of children, was well known; however, this group was also rapidly mobilized, which may have had beneficial effects.

Although early studies suggested that the young male and older female were the most severely affected by acute polio, this was not reflected in the incidence of new problems in our study.

Our data, overall, most closely agree with those of Codd and co-workers [5]. Both of these studies, however, involved Minnesota populations, with some similarity in treatment, and were not self-referred or symptomatic in their initial selection. The incidence of pain and cramping in Codd's study (48%) is similar to our study, in which 47% report this problem. Perhaps of more significance is the similarity in both studies of the proportion reporting increased weakness in previously affected and in new areas. Only 15%–16% report recent weakness confined to previously unaffected areas, with 20%–30% finding both old and new areas affected, and 50%–66% feeling that the recent weakness is limited to previously affected areas. The problems of self-reporting and clarifying initial involvement are acknowledged. Comparison with the original 1952 to 1953 hospital records as well as current clinical evaluation are needed to further define new post-polio symptoms.

Overall, new problems 30 or so years after polio onset appear to occur in 20%–40% of respondents to questionnaires who previously had not been self-referred to a support group or clinic. This latter population has been shown to be more symptomatic; however, they also comprised a subgroup of patients older at onset, with presumably more severe disease; both of these characteristics have been shown by this study and Codd's to be associated with an increased incidence of problems.

Larger studies with access to medical records and clinical evaluation of the current status of individuals with polio will need to be completed to allow the most accurate prediction of the expected incidence of problems. Indeed, this present group later may show increasing incidence of post-polio sequelae. Further follow-up studies of this group and others are planned.

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The Importance of Symptom Pattern in Evaluating Post-Polio Neuromuscular Changes

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Many patients develop new neuromuscular symptoms decades after recovery from acute paralytic poliomyelitis [1, 2]. Symptoms vary in their nature, severity, and location. They may arise in many different muscle groups, whether or not affected by polio originally. These symptoms, whether they progress or not, are of great concern to the patients and have been difficult to evaluate [2-4]. In some patients, the weakness is progressive and has been termed progressive post-poliomyelitis muscular atrophy [2].

We have attempted to evaluate the importance of different symptom patterns in patients complaining of neuromuscular changes years after polio. We have observed a large number of patients coming to clinic with a variety of symptoms. The medical literature does not document well the importance of these different symptoms [2-5]. We also wanted to determine the best way to evaluate these symptoms using commonly available clinical staff and facilities. We plan to follow patients to see the progression of symptoms and signs over the next few years. We are reporting here on our preliminary results from evaluating initial symptoms of the first 50 patients coming to clinic.

METHODS

All patients were referred to the clinic either by their primary physician or themselves. We developed a detailed questionnaire to have the patients document their symptoms before coming to clinic. We wanted to look at the frequency of symptoms, the pattern and time course of their appearance, related problems, functional deficits, and areas of concern to patients. Our plan is to do reliability and validity studies of the questionnaire responses, follow the patients over time, and then observe if symptom patterns correlate with progression of weakness or other problems.

Patients were evaluated with a history and physical examination, which included neurologic, musculoskeletal, and functional evaluation. After this examination, patients were referred for diagnostic tests and consultations, as indicated by their history and physical findings. Diagnostic tests commonly included electromyographic studies, muscle enzyme, and other lab tests. Consultations were frequently obtained from other medical specialties, physical therapy, occupational therapy, orthotics, psychology, and vocational rehabilitation. In addition, several patients required neurologic and orthopedic consultation. We attempted to quantify the degree of weakness with objective measures of strength and physical therapy and occupational therapy where indicated.

Those patients who appeared to have a progression of weakness not explainable by other causes or who needed to have other diagnoses ruled out were referred for electromyographic studies. In addition to looking at motor unit amplitude, duration, and shape to assess the extent of old polio involvement, we looked at motor unit function. We knew that patients with a history of polio often had membrane instability not only in obviously affected muscles, but also in muscles previously not realized to have been affected [5]. We had originally felt that the size of fibrillation potentials would correlate with new denervation of muscle fibers, but found that it did not even discriminate very well between symptomatic and asymptomatic muscles. Therefore, we did quantitative motor unit analysis using a monopolar needle, delay line, and trigger to examine in detail motor unit action potentials for complexity and stability. Single fiber EMG and open muscle biopsies were not done, nor did we routinely do psychologic testing. We did not have examiners who were blinded to patient symptoms. We wanted to use the standard clinical staff and tests because this was a study to help with clinical evaluation of patients presenting with symptoms.

RESULTS

The average age of patients presenting to clinic with new symptoms was 49. This is similar to the estimated population of patients in state of Washington who had polio between 1946 and 1960. With the assistance of the state epidemiologist, Health Department records were reviewed. This review revealed that approximately 6,500 state residents had polio during those years. Without adjusting for death or patients moving out of state, their most frequent age was 42 in 1985.

After thorough evaluation of 50 consecutive patients, we found 3 patients who had other diagnoses as the cause of most of their symptoms. One patient was found to have bilateral aseptic necrosis of the hips, with a need for total hip replacements after x-ray and orthopedic evaluations. A second patient was

found to have multiple sclerosis after somatosensory evoked potentials, visual evoked potentials, and neurologic evaluation. A third patient was found to have myotonic muscular dystrophy with a previous history of this illness and previous evaluation by neurology. These patients were excluded from further analysis by the questionnaire and findings on examination, though they all did state that they had had polio as children. One patient met our predetermined criteria for progressive post-polio muscular atrophy because he had a previous history of polio, no other diagnoses, clear progression of weakness, and the predetermined electrodiagnostic criteria. His large motor units were consistent with previous polio, and he had large positive waves, fibrillations, and unstable motor units on quantitative motor unit analysis. It is possible that other patients who have not had enough time to return for follow-up and demonstrate weakness on examination are also having progressive weakness. We are not able to say that the symptoms, signs, or tests we looked at will predict who will have progressive weakness. Perhaps single fiber electromyography and open muscle biopsies would contribute additional information.

We found that patients were complaining of a variety of symptoms and symptom patterns; 74% complained of new weakness or fatigue that on the average began 30.5 years after their original illness (standard deviation [SD] 15.9); 76% complained of aches and pains in their muscles 26.8 years later (SD 17.5); and 38% complained of twitches and tremors in muscles 18.1 years later (SD 18.5). The symptoms were most commonly in muscles previously affected with polio and subjected to much use during ambulation or while using a cane. The symptoms, such as weakness and pain, usually began within one year of each other, but there was much variability, and no clear pattern appeared where one symptom preceded another. More of the symptoms occurred in a lower limb muscle, but again, there was much variability, and the spread of symptoms to other limbs and muscles did not follow a consistent pattern either. One fairly common pattern was for the symptoms to appear later in the opposite lower limb and then, occasionally, in the upper limb on the same side.

In addition to many complaints of new symptoms, there were many patients who had had significant functional losses. Of 46 patients whose questionnaires were appropriate for analysis, 36 complained of new difficulty with walking, 34 with stairs, 25 with transfers, 24 with work, 23 with homemaking, 12 with driving, 10 with respiratory ability, and 8 with dressing. Forty-five percent (45%) complained of some emotional difficulty whether or not related to their new symptoms. It is very likely that there was some overreporting of symptoms in patients with emotional problems, but we did not have the ability to obtain psychologic testing on all subjects. Several subjects were referred for appropriate counseling. There also may be some subjects who did not come to clinic but who have significant symptoms and

functional losses. Several patients stated that they would have obtained evaluation earlier if facilities had been available.

We also looked at the most frequent type of question that patients had about their illness. Almost all the patients wanted information and evaluation for their symptoms. Eighty-six percent wanted to know specifically whether exercise would be helpful. A large number also had questions about equipment, but few patients had questions about work, attendant care, transportation, finances, or emotional stress.

On examination, the patients were found to have a severe amount of weakness and multiple secondary complications. Finding the weakest muscle group in each limb by manual muscle test score (0–5), we then added the four scores to get a total score (0–20). This score emphasizes the amount of weakness. A normal subject would have a score of 20, but a subject with one muscle of grade 4 would have a total score of 19 ($19 = 5 + 5 + 5 + 4$). The average score was 14.8 with a SD of 3.2. We also evaluated for contractures in 8 joints. Eighty percent of the patients had a contracture in one or more joints. One patient had contractures in 6/8 joints checked, and the average patient had 1.75 contractures with a SD of 1.5. Sixteen percent of the patients had clinically significant recurvatum at the knee, 22% had a lower limb at least one inch shorter than the other, and 42% had an obvious scoliosis on examination. There was a large amount of variability in the physical findings, and there were no striking correlations between symptoms and physical findings. As would be expected, we did find more secondary mechanical problems in the weaker lower limbs, but the severity of symptoms did not correlate well with amount of weakness on examination. Analysis of this preliminary data did not reveal a correlation between severity of symptoms and severity of initial illness, though it is known from other studies [1] that severity of initial illness is, in general, worse in those patients who do develop symptoms.

We wanted to evaluate the amount of intervention needed for these patients. Forty-two percent were referred for electrodiagnostic testing. We did not find that electrodiagnostic results correlated well with location or severity of symptoms, but did feel it was helpful to rule out other diagnoses, to assess the extent of muscle involvement, and to guide therapy. Sixty percent of the patients were referred for physical therapy, most commonly for gait training, use of equipment, or strength testing; 20% had a new orthotic device prescribed, and 9% had a significant replacement or repair. Thirteen percent had a lift prescribed, and another 13% had a cane or crutch prescribed. Only 11% were referred to occupational therapy, which, on reviewing our data, we felt that we had underutilized. It appears that more psychologic and vocational assessment and counseling may be indicated.

DISCUSSION

These data represent an attempt to assess the importance of symptom pattern in patients presenting with complaints after polio. We were limited by several significant methodologic problems. These patients were referred by their primary physician or were self-referred. The extent of psychologic bias of subjective responses was not quantified. There is no single, well-accepted, objective measure of progressive weakness other than strength testing over several years. We plan to collect more data from subjects and follow-up examinations. The difficulty the subjects have in accurately describing the location of symptoms was apparent as we reviewed their initial description with them. Often joint and ligament symptoms were confused with muscle symptoms and the location was imprecise. Due to the great variability of symptoms and their susceptibility to subjective biases, symptom reports alone are not adequate to study progression of weakness.

There does appear to be a similar pattern of symptoms occurring about three decades after polio. Weakness, fatigue, and pain are causing this group of patients significant functional changes and distress. It is very important, therefore, to rule out other diagnoses, document their status, and address their mechanical, functional, and emotional problems. Thorough serial examinations are needed to document progression of physical signs and functional changes because objective tests do not reliably predict them. More study of symptom patterns and clinical findings is needed with careful control for biases in order to predict progression of symptoms and guide therapy.

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Dysphagia in Post-Polio Patients

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INTRODUCTION

Difficulty in swallowing (dysphagia) occurs in 10% to 15% of patients with acute paralytic poliomyelitis [1]. Among 201 post-polio patients responding to a questionnaire, 22% reported new difficulty with eating or swallowing at a median duration of 34 years following their acute illness [2]. Beyond these facts, little is known about dysphagia in post-polio patients.

Severe dysphagia poses life-threatening consequences such as aspiration pneumonia and asphyxia. Even mild dysphagia results in a daily struggle to maintain adequate hydration and nutrition. In many cases, dysphagia is remarkably "silent," with minimal symptoms despite consistent airway penetration by swallowed material. Silent dysphagia can lead to catastrophe without warning.

The post-polio population in the United States totals 200,000–250,000, according to estimates of the National Center for Health Statistics. Assuming that 10% to 15% of this population had bulbar polio, there could be 20,000 to 37,500 survivors of bulbar polio in this country alone. The actual number may be lower if bulbar polio patients have been more likely than nonbulbar ones to die from complications of their disease.

The extent of recovery from dysphagia among bulbar polio survivors is unknown, but the persistence and recent recrudescence of other disabilities in post-polio patients raises the specter of many thousands of individuals afflicted with residual post-polio dysphagia. The prevalence and severity of post-polio dysphagia may be on the rise, judging from experience with other late effects of poliomyelitis. Improved understanding and management of this problem is sorely needed.

Thirteen post-polio patients with dysphagia have been studied by The Johns Hopkins Swallowing Center, which is a multidisciplinary effort involving specialists in radiology, gastroenterology, otolaryngology, rehabilitation medicine, speech-language pathology, and neurology [3]. A patient is seen by one or more clinicians who are selected according to the patient's type of

swallowing problem. Each patient undergoes dynamic imaging of swallowing by means of cinepharyngoesophagography. This technique provides an x-ray motion picture of the patient's oral cavity, pharynx, and esophagus while swallowing barium. The film is exposed at a rate of 16 to 24 frames per second, and it can be played back as slowly as one frame at a time in order to visualize the complex, rapid movements of swallowing. Standard barium swallow examination is directed to the esophagus, revealing little information about oral and pharyngeal function, which is of primary interest in post-polio patients.

The goals of the Swallowing Center evaluation are to diagnose the cause(s) of dysphagia and to establish a treatment plan that may be carried out by the Swallowing Center staff or by the referring physician. The 13 patients with post-polio dysphagia were routine referrals among the approximately 150 patients seen yearly at the Swallowing Center between 1982 and 1986. This paper describes the findings of historical, neurologic, and cineradiographic examinations of these patients.

HISTORICAL FINDINGS

Of the 13 patients, 10 were male and 3 were female. The age range at the time of evaluation was 40 to 75 years, with a median age of 54 years. The age range at the time of acute polio was 2 to 33 years, with a median age of 12 years.

Eleven of the 13 patients had fair-to-good recall of their acute illness. The other 2 patients were 2 and 5 years old at the time of illness and 70 and 75 years old, respectively, at the time of evaluation. All 13 patients were judged to be reliable historians regarding events subsequent to the acute illness. Medical records pertaining to the acute illness were not reviewed, because the records were generally unavailable.

Nine of 11 patients initially experienced severe bulbar dysfunction, and over half of these patients required tube feeding, tracheostomy, and/or mechanical ventilatory assistance. Two patients described only mild dysphagia at disease onset. Limb weakness, usually quadriplegia, was present in 11 patients. Ten patients were hospitalized, and one was treated at home.

All 13 post-polio patients were able to recall their condition at the time of maximal recovery several years after the acute illness. Eleven had mild residual dysphagia with variable characteristics as described below. Five had mild residual slurred or hoarse speech, and 4 had mild-to-moderate limb weakness, one needing a full leg brace. None of the patients had noteworthy respiratory symptoms following recovery.

Some of the 11 patients with residual dysphagia had difficulty mainly with solid food particles occasionally becoming stuck in the hypopharynx,

requiring forceful coughing or retching to dislodge the material. Troublesome solids included tough meats, crisp fruits and vegetables, popcorn, nuts, peanut butter, and medication tablets. Other patients had greater problems with liquids causing cough/choke episodes and laryngospasm. Nasal regurgitation of liquids was often noted, especially when drinking from a water fountain. Difficulty with oropharyngeal secretions tended to occur while lying supine, typically presenting as nocturnal awakenings with choking.

None of the patients reported severe dysphagia complications in the past, such as recurrent pneumonia or frequent airway obstruction episodes. The absence of unfavorable outcomes in this group partly reflects the likelihood that most patients with severe dysphagia complications already have died as a result. However, avoidance of complications also represents successful compensation for dysphagia [4]. Compensation is partly involuntary, in the form of enhanced muscular contraction in one part of the pharynx to adjust for weakness in another part. Compensation can also be voluntary, in which case there are historical clues. For example, most of these patients reported altering their diet to avoid difficult-to-swallow solids such as nuts, and liquids such as carbonated soda. The patients tended to cut solids into small pieces, chew thoroughly, take small sips of liquids, and eat slowly. Some of them discovered that swallowing was easier with the head turned to one particular side, and one patient benefitted from applying manual pressure to one side of the neck while eating. By using these forms of voluntary compensation, patients largely avoided dysphagia symptoms. Unfortunately, patients and their physicians thereby can be misled into a false sense of security, and sudden, unexpected decompensation such as aspiration pneumonia can occur if there is even slight additional compromise of swallowing performance.

Nine of the 13 post-polio patients reported progressive dysphagia, and 2 of these 9 had not had swallowing problems for decades following maximal recovery. Progression entailed not only increasing frequency and severity of previous dysphagia symptoms but also onset of new dysphagia complications. These complications included airway obstruction episodes requiring Heimlich maneuver, recurrent bronchospasm due to airway penetration by liquids, and aspiration pneumonia.

The duration of progression in 8 of the 9 progressive dysphagics ranged from 6 months to 3 years prior to the Swallowing Center evaluation. The latency from acute illness to onset of progression ranged from 28 to 69 years with a median latency of 33 years, similar to the other progressive post-polio symptoms. One patient described very gradually progressive dysphagia over 30 years, beginning shortly after his maximal recovery from acute polio.

Coincident with progressive dysphagia, these 9 patients generally noted progressive speech difficulty. Speech was variably described as more hoarse, slurred, and/or weak. Five of the total group of 13 post-polio dysphagia

patients also complained of recent progressive fatigue, limb weakness, and joint and/or muscle pain. Four of these 5 were among the 10 patients with progressive dysphagia symptoms. No patient complained of increasing respiratory impairment other than acute dyspnea episodes related to airway penetration while swallowing. No patient had symptoms consistent with sleep apnea.

There was no unusual occurrence of other medical problems in the total group of 13 post-polio patients except for depression necessitating prior psychiatric treatment in 3 and Parkinson disease in one. The patient with Parkinson disease developed that condition several years before experiencing progressive dysphagia. This patient's Parkinson disease was only mildly symptomatic with medication, and such mild Parkinsonism is not usually associated with symptomatic dysphagia. The new insult of Parkinson disease added to the old injury of bulbar polio may have caused his progressive dysphagia, rather than an effect of Parkinsonism or polio alone.

NEUROLOGIC FINDINGS

By physical examination, nearly all 13 patients had evidence of palatal, pharyngeal, and laryngeal weakness (Table 1). Asymmetric palatal rise and/or lateral deviation of the posterior pharyngeal wall with phonation were almost always easily seen. Speech was usually impaired in the form of slurring or hoarseness. Diffuse face and tongue weakness was occasionally found. Although mild swan-neck posture and scoliosis were common, swallowing did not seem to be compromised by these skeletal deformities, which did not require bracing.

Only one patient had upper motor neuron signs, including hyperactive gag and jaw jerk reflexes and bilateral Babinski signs. This condition has substantially deteriorated during 3 years of observation with serial neurologic examinations and 4 cineradiographic studies, and the patient probably has coinciding amyotrophic lateral sclerosis rather than a progressive post-polio disorder.

TABLE 1. Neurologic Examination

Asymmetric palate and/or pharynx	12/13
Dysarthria/hoarseness	11/13
Limb abnormalities	6/13
Swan-neck posture	5/13
Scoliosis	5/13
Facial weakness	5/13
Tongue weakness	2/13
Upper motor neuron signs	1/13
Parkinsonism and orthostatic hypotension	1/13

CINERADIOGRAPHIC FINDINGS

Pharyngeal constrictor muscles were atrophic and weak in 11 of the 13 patients (Table 2). Weakness was manifested in several ways. Most commonly, there was diminished peristaltic pumping of the barium bolus, and, sometimes, no pharyngeal constrictor muscle contraction was visible. Weakness was often asymmetric, in which case the barium passed down one side of the pharynx. Reduced clearance of barium from the pharynx into the esophagus resulted in retention of barium in the pharyngeal recesses (valleculae and piriform sinuses). Pharyngeal weakness was also seen as excessive pharyngeal laxity allowing ballooning of the pharyngeal walls with insufflation. In some instances, lateral pharyngeal pouches had developed as a result of pharyngeal constrictor weakness, although the pouches themselves were not felt to be causing dysphagia symptoms.

Barium consistently penetrated the larynx in over one-half of the cases. This resulted mainly from impaired downward movement of the epiglottis and diminished upward movement of the larynx. In every case with laryngeal penetration, the penetration did not result in coughing. Normally, violation of the larynx by foreign material triggers a cough reflex. This reflex is often lost in long-standing laryngeal penetration by almost any cause. Presumably, either local sensory mechanisms are damaged by chronic inflammation, the central nervous system becomes habituated to the triggering stimulus, or both.

Regardless, loss of the cough response to laryngeal penetration has two major consequences. First, laryngeal penetration occurs *silently*, without knowledge to the patient or the physician. Accordingly, the presence and severity of dysphagia may be grossly underestimated. Complications such as airway obstruction and aspiration pneumonia may occur suddenly, without warning, and sometimes without recognition that there is underlying chronic impairment of swallowing. This is especially true if the patient has largely compensated for dysphagia and if a history of the symptoms of voluntary compensations (see above) is not specifically sought.

Second, the reflex cough is an important lung clearance mechanism.

TABLE 2. Cinepharyngoesophagography

Pharyngeal constrictor weakness	11/13
Esophageal dysfunction	8/13
Pharyngeal laxity/pouches	7/13
Laryngeal penetration	7/13
Pharyngeal and/or palatal asymmetry	6/13
Epiglottic dysfunction	5/13
Difficulty initiating swallowing	5/13
Nasopharyngeal reflux	4/13
Obstructing esophageal lesion	1/13

Without it, material that enters the airways is more likely to be retained and cause further complications.

Gastroesophageal reflux and disordered esophageal motility were common findings of cineradiography in the 13 post-polio patients, often without symptoms of heartburn, sour regurgitation, and chest pain. Since esophageal dysfunction can be found in healthy, asymptomatic subjects, its presence in these post-polio patients is likely coincidental and insignificant. The patients' symptoms were primarily of pharyngeal, not esophageal, dysphagia, and virtually all patients had corresponding pharyngeal abnormalities by cineradiography.

One patient was found to have an unsuspected, obstructing, upper esophageal stricture [5]. He was a 44-year-old man who had had bulbar polio at age 9 requiring tracheostomy and prolonged nasogastric tube feeding. After recovery, he had mild but slowly progressive dysphagia, with solid foods occasionally sticking at the base of his throat. Cinepharyngoesophagography demonstrated moderate diffuse pharyngeal paresis causing pharyngeal retention and mild laryngeal penetration of barium. A tight upper esophageal stricture was also discovered, and it was noted to be causing a "jet-effect" in the barium stream, suggesting that the stricture was producing obstructive symptoms. The stricture was presumed to have resulted from prolonged nasogastric intubation during the acute polio illness.

The stricture was successfully dilated, as confirmed by repeat cineradiography, and the patient's symptoms fully resolved, *despite* persistent pharyngeal paresis. He could eat previously avoided foods such as apples, and he was able to finish meals as quickly as his family. His chronic dysphagia symptoms, long attributed to post-polio pharyngeal weakness, were in fact due to a treatable obstructing esophageal lesion. This case reinforces the value of cinepharyngoesophagography, because the stricture and jet-effect were not seen on the fluoroscope during the study but were appreciated at the time of frame-by-frame film review.

CONCLUSIONS

Post-polio dysphagia is a problem affecting thousands of individuals in the United States alone, and its consequences range from annoying to life-threatening. Of 13 patients who sought evaluation for this problem, 9 reported progressive symptoms, suggesting that post-polio pharyngeal muscle weakness may worsen beginning approximately 30 years after the acute illness. As yet, however, objective studies such as serial cinepharyngoesophagography have not been done to document this impression. Longitudinal studies of this sort will be helpful in determining whether or not post-polio dysphagia is a truly progressive disability.

Other studies regarding the prevalence and characteristics of dysphagia in a larger post-polio population are also needed.

When confronted with an individual post-polio patient with dysphagia, the clinician should strongly consider obtaining dynamic imaging of swallowing, either cineradiography or videofluoroscopy. This is especially true if dysphagia symptoms are progressive or severe (such as episodes requiring Heimlich maneuver, or aspiration pneumonia). Treatable causes of dysphagia such as obstructing lesions may be found. Only with dynamic imaging can the true extent of dysphagia be assessed, because history and physical findings often underestimate its severity. Dynamic imaging findings can also provide essential feedback to the swallowing therapist, who may be able to relieve post-polio dysphagia by modifying food characteristics and swallowing posture.

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DISCUSSION

DR. ANTEL: Using your rather sophisticated techniques, can you quantitate in some way the amount of muscle involvement and do any of the patients complain of pain on swallowing?

DR. BUCHHOLZ: To answer the latter question first, no patient has com-

plained of pain. With regard to the former question, we have not been able to figure out a way to quantitate the amount of muscle involvement. On the other hand, we can do serial studies and make observations comparing a film from a year ago to one done today and see a visible difference which, I think, is fair objective evidence.

DR. JOHNSON: In those 5 out of 13 that had weakness of their epiglottis, were any of them evaluated in a sleep lab?

DR. BUCHHOLZ: I do not believe any of these patients have been evaluated in a sleep laboratory. I also am a sleep disorders specialist. I am a polysomnographer, so I am fairly sensitive to sleep apnea. I asked carefully for symptoms of sleep apnea in these cases and came up empty handed. These patients, however, certainly would seem to be at risk for sleep apnea.

DR. HALSTEAD: I have a concern about the issue of silent dysphagia. As a clinician who sees a lot of polio patients, which patients do I select for videofluoroscopy and which patients are really at risk for developing symptomatic nonsilent problems?

DR. BUCHHOLZ: I do not yet really know the answer. I have been amazed at the ability of the lungs to clear penetrated or aspirated material. We routinely see patients in the Swallowing Center with a variety of neurologic disorders causing swallowing compromise. These patients often penetrate the larynx with every swallow. Some of them will pour material into their trachea and down into their lungs. They are obviously doing that every time they eat, not just when they do the study, and yet these patients have normal chest x rays. Most of them have not been carefully studied with pulmonary functions, but they do not report a history of recurrent bronchospasm or pneumonia. It is hard to know then what puts someone at risk of a serious event. My advice would be to study those patients in whom the dysphagia seems to be particularly troublesome, those who are able to eat only a restricted diet with great difficulty or those in whom the problem is progressive. I think it is also important to keep in mind that, just as other aspects of a disabled individual's function may be assisted with rehabilitation, so may swallowing. The kind of guided modification of diet and feeding posture that I mentioned, using videofluoroscopy to look at these patients, not only affords an opportunity to see how compromised they are, how much risk they may be facing, but also perhaps to give them some assistance in feeding more easily and more safely. The people who are able to do swallowing rehabilitation are Speech-Language Pathologists, Rehabilitation Medicine specialists, and Occupational Therapists.

Amyotrophic Lateral Sclerosis and Post-Polio: Differences and Similarities

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INTRODUCTION

Post-poliomyelitis muscular atrophy (PPMA) is the new muscle weakness that develops in some patients with old poliomyelitis many years after the original illness [1-4]. The clinical, electrophysiologic, immunologic, virologic, and muscle biopsy characteristics of PPMA patients previously described [1-5] suggest that PPMA is a slowly progressive form of lower motor neuron deterioration. Although it has been said that amyotrophic lateral sclerosis (ALS) is more frequent among patients with old polio [6, 7], our recent studies do not support such observations [3].

ALS is the prototype of motor neuron diseases of unknown cause. PPMA is the new lower motor neuron deterioration that occurs in patients with long-standing lower motor neuron deficit caused originally by a known virus. Although clinically these 2 conditions are different, at the cellular level, both ALS and PPMA have dysfunction of the lower motor neurons in common. Comparison, therefore, of ALS with PPMA could help in their differential diagnosis, especially when symptoms and signs appear to overlap. Furthermore, such a comparative analysis may raise questions of special neurobiologic interest such as: 1) Are there anatomic, virologic, immunologic, or serologic differences between a known, post-viral motor neuron disease (PPMA) as opposed to an acquired, progressive motor neuron disease of unknown etiology (ALS)? 2) What is the long-term viability and function of a motor neuron that survived or escaped acute insult from the polio virus? 3) What is the life-span of an over-functioning motor neuron that has been stressed for years to compensate for the lost neurons? and 4) Are there differences between ALS and PPMA in the metabolic activity of the cortical neurons?

METHODS

For the comparative analysis, at least 60 PPMA patients, mean age 46 years (range 31–68), were studied at the Clinical Center, National Institutes of Health, after giving informed consent. Some post-polio patients had also been studied earlier during an initial admission at the NIH between 1960 and 1981 and were reexamined in 1985 as part of our long-term follow-up study [3].

All the post-polio patients had a history of acute paralytic poliomyelitis in childhood or adolescence, documented as well as possible by the clinical occurrence of an acute febrile illness followed by paralysis. In addition, neighborhood or school epidemics were checked. Patients who were affected in the United States were selected, particularly from the later epidemics, when the diagnosis of poliomyelitis was probably made with more accuracy. The PPMA patients enrolled in the study fulfilled the following criteria: They had partial recovery of motor function after polio and functional stability or recovery for at least 15 years; they had residual muscle atrophy, weakness, and areflexia in at least one limb but with normal sensation; they had new symptoms such as muscle weakness and areflexia in at least one limb, but with normal sensation; and they had new symptoms such as muscle weakness, atrophy, fasciculations, and fatigue unrelated to any other neurologic or medical disorder. Patients with symptoms due to injury, compression neuropathy from the use of crutches or wheelchairs, or radiculopathies were excluded.

Patients with ALS had a progressive disease confined to lower motor neurons or more often, a combination of upper and lower motor neuron disease. None of the ALS patients selected at random had a history of a prior paralytic disease such as poliomyelitis. The ALS was rapidly progressive in most of the patients and fulfilled the criteria for diagnosis as previously described [8]. Patients were excluded from both groups of ALS and PPMA if they had diabetes, polyneuropathy, collagen vascular disease, exposure to toxic agents, other major viral illnesses, or a family history of a neuromuscular disease.

All the patients included in the comparative study had the following detailed examination:

- 1) Serial clinical neurologic exams during the initial and subsequent follow-up visits to assess degree and rate of progression of the neurologic signs and symptoms.
- 2) Routine blood chemistry including determination of muscle enzymes, complete blood count, vitamin levels, serology, toxicology, quantitative immunoglobulins, and immunoelectrophoresis.
- 3) Examination of the lymphocyte subsets using monoclonal antibodies that identify surface membrane markers [9, 10].

- 4) Search for circulating antineuronal antibodies to spinal cord neurons using the immunoperoxidase or immunofluorescent technique [11–13].
- 5) Determination of antibodies to poliomyelitis virus, herpes, cytomegalovirus, measles, and human lymphotropic virus I and III (HTLV-I, HTLV-III) in both serum and spinal fluid (CSF). Specific IgG viral synthesis in the CSF was calculated for the polio and other viruses [14].
- 6) Examination of the CSF for oligoclonal bands by high resolution agarose gel electrophoresis and immunofixation [15, 16].
- 7) Open muscle biopsy, processed for muscle enzyme histochemistry [1, 5]. In PPMA patients, the muscle biopsy was taken from a newly weakening muscle that was previously affected and had partially or fully recovered, or from a newly weakening muscle that was clinically unaffected historically during the original illness [5]. Five asymptomatic post-polio patients were also biopsied for comparison [5]. In ALS patients, muscle biopsy was performed from a nonclinically affected muscle to determine subclinical involvement of motor neurons in a disease thought to be generalized, or from a slightly weakening muscle. End-stage muscles or muscles with severe deficit and significant atrophy clinically were rarely biopsied.
- 8) Electromyography (EMG), including quantitative studies of the voluntary motor units and spontaneous activity. Single fiber EMG was also performed in some PPMA patients, and the results were compared with the single fiber EMG data from ALS patients [17].
- 9) Histology of the spinal cord stained with H & E and for myelin in patients with classic ALS, patients with PPMA, and patients with stable post-polio without new weakness who died from unrelated causes [18].
- 10) Positron emission tomography (PET) of the brain measuring the utilization of ^{18}F -2-deoxy-D-glucose in the cortical, basal ganglia, and cerebellar neurons [19], in an attempt to find differences in glucose utilization between ALS with and without upper motor neuron involvement and patients with PPMA who lack upper motor neuron signs.

RESULTS

Clinical Characteristics

In PPMA, the new muscle weakness, with or without atrophy, is found in few muscle groups, more often in muscles that had been previously affected and had fully or partially recovered [1–5]. In PPMA, the new weakness is

usually asymmetric and appears to remain asymmetric as the disease progresses [3]. Fasciculations may be present, especially in the newly weakened muscles, but also in some stable muscle groups. Muscle pain of neurogenic type [20], present in some PPMA patients, is different from the joint pain or the pain due to osteoarthritis that some post-polio patients also experience [1, 2, 4, 21]. Very often, there is a combination of joint and muscle pain, and at times, there is no clear distinction between the two. The progression of these symptoms is generally very slow, estimated to be 1%/year of the total neuromuscular function, often with 1 to 10 years of relative stability [3]. A representative course and progression for 4 PPMA patients is shown in Figure 1. These patients do not have or develop upper motor neuron signs [1–4, 21], although very rarely, an occasional, isolated Babinski sign has been seen.

In contrast, symptoms and signs of ALS may start focally, but when patients are examined, signs of more generalized disease are found or develop in a very short period. The progression of ALS is much faster, as shown in Figure 2 for 5 ALS patients and one PPMA patient followed up for the same period during an experimental trial with interferon [22]. Bulbar and respiratory muscle involvement are invariably present or develop in ALS patients, and in contrast with PPMA, ALS is always fatal. Although some new bulbar and respiratory symptoms may develop in PPMA patients, this is the exception and not the rule [21]. In PPMA, the severity of the new symptoms, in reference to the resulting new disability, depends on the residual deficit the patients had at their “starting point.” For example, a post-polio patient who has been left with severe residual deficit of bulbar or respiratory muscles can experience new respiratory or bulbar symptoms if PPMA develops and affects these muscles. In such a patient, however, the symptoms should not be interpreted as ALS. Although we have seen very few such patients, their progression is anticipated to be the same as that we reported for the limb muscles in PPMA [3]. If the respiratory muscle reserves in such rare post-polio patients are, however, very minimal, even mild new progression could have a major impact on this patient’s life-span. In contrast, none of our large number of PPMA patients who had residual deficits confined only to the limbs developed bulbar or respiratory muscle weakness resembling ALS, even during our long-term follow-up study [3]. Therefore, it is safe to state that the prevalence of ALS is not higher in post-polio patients, and the clinical symptomatology of PPMA is different than that of ALS not only in the rate of progression and the anticipated disability, but also in the distribution of the new weakness. While ALS is a generalized motor neuron disease, PPMA remains predominantly focal or multifocal, affecting certain muscle groups.

Chemistry and Virology in Serum and CSF

Routine blood chemistries are normal in both ALS and PPMA patients. The serum CK can be elevated up to 1,000 units (normal up to 200) in some

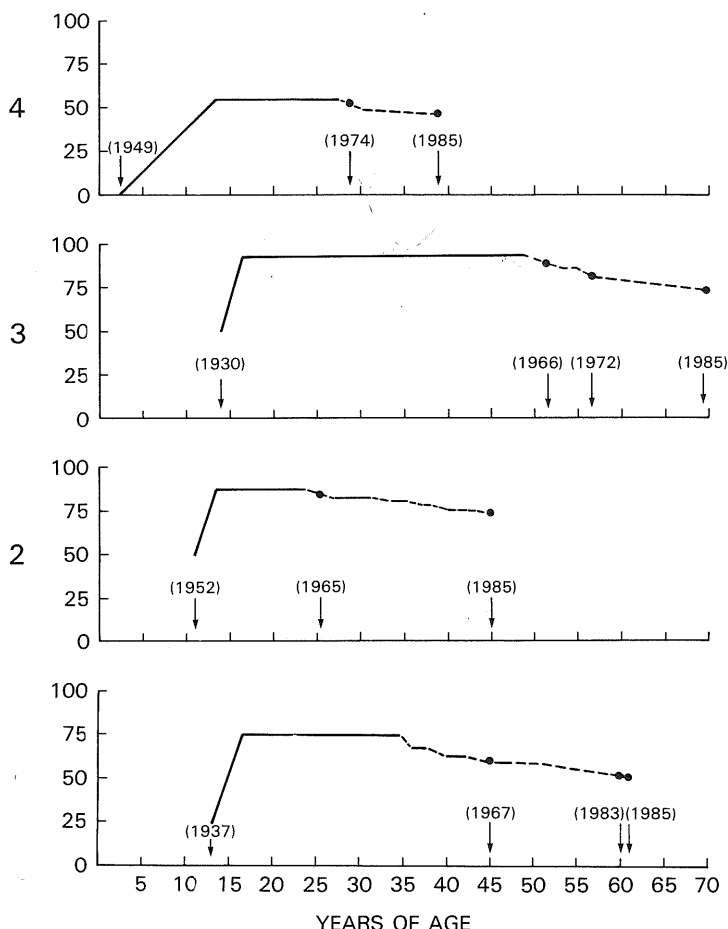


Fig. 1. Progression of muscle weakness in 4 patients with post-poliomyelitis muscular atrophy, expressed as total points of estimated neuromuscular function at various years of age. Numbers on the left refer to individual patients. Points of muscular function (100 points is normal strength in all 4 limbs) [3, 21], are on the ordinate. The continuous line represents the patients' course after the attack of acute polio and their progressive partial recovery with subsequent long stabilization, as determined from information provided by the patients or early records. The interrupted line represents the course of new muscle weakness from onset until the latest follow-up evaluation. Arrows with the years in parentheses represent time of the acute polio attack (first arrow), the time of the first examination after the manifestation of new weakness (second arrow), and subsequent examinations (third or fourth arrow). A decline in muscular strength that was either continuous or that occurred in a stepwise fashion took place in all the patients between the first and last evaluations.

ALS patients, especially those with more rapidly progressive disease (Dalakas, unpublished observations). This is, however, also true for some PPMA patients who may have a persistent elevation of CK and other muscle enzymes up to fourfold [1-4, 21]. Caution should be exercised not to confuse such a finding with a sign of possible inflammatory myopathy, especially when inflammation can be seen in the muscle biopsies of some PPMA patients [5, 21]. Clinical correlation and proper judgment should help the clinician to decide whether there exists such a rare combination of PPMA with a concomitant inflammatory muscle disease. We believe the reason for CK elevation in PPMA is not only the mild inflammation, but also the presence of "myopathic" features, as we and others have found in muscle biopsies due to the long-standing residual denervation atrophy [5, 21, 23]. The elevated CK has at the moment no diagnostic or prognostic significance. We have treated 2 patients with PPMA, elevated CK, and muscle inflammation with immunosuppressive agents without success (Dalakas, unpublished observations). Inflammatory changes are very rare in ALS, as discussed below.

The total serum immunoglobulins and immunoelectrophoresis in PPMA patients are normal; this is in contrast to ALS patients, who have a rare, associated monoclonal gammopathy of unknown significance [24]. Viral antibody titers in both serum and CSF were examined by ELISA for measles virus (Edmonston strain) and cytomegalovirus (CMV) [1-3]. Antibodies to herpes virus type 1 (McIntyre strain) and type 2 (multiple sclerosis strain), toxoplasma gondii, retroviruses and CMV (strain AD/69) were also examined by indirect hemagglutination inhibition (IHA) technique [1-3]. Poliovirus neutralizing antibody titers to type 1 (Maloney strain), type 2 (mouse embryo fibroblast strain), and type 3 (Sankett strain) were also examined in both serum and CSF [25], and the extent of poliovirus antibody production inside the blood-brain barrier (BBB) was determined by making a correction for BBB permeability using the CSF:serum albumin ratio [14]. No specific elevation of viral antibodies was found in the patient's serum or CSF. Although post-polio patients as expected had antibodies to the polio virus in the serum, no specific elevation of antibodies to the poliovirus was found in the CSF of PPMA patients when the BBB permeability was corrected.

Immunology in Serum and CSF

Analysis of lymphocytes with monoclonal antibodies in as many as 28 PPMA patients and up to 20 ALS patients failed to reveal a specific immunoregulatory cell abnormality. As we have reported previously [1, 2], 8 PPMA patients had an abnormal helper/suppressor ratio (increased or decreased). These changes were not, however, internally consistent, and their significance is unknown. More recent studies in our laboratory did not show any changes in the lymphocyte subpopulation in our PPMA patients. Only

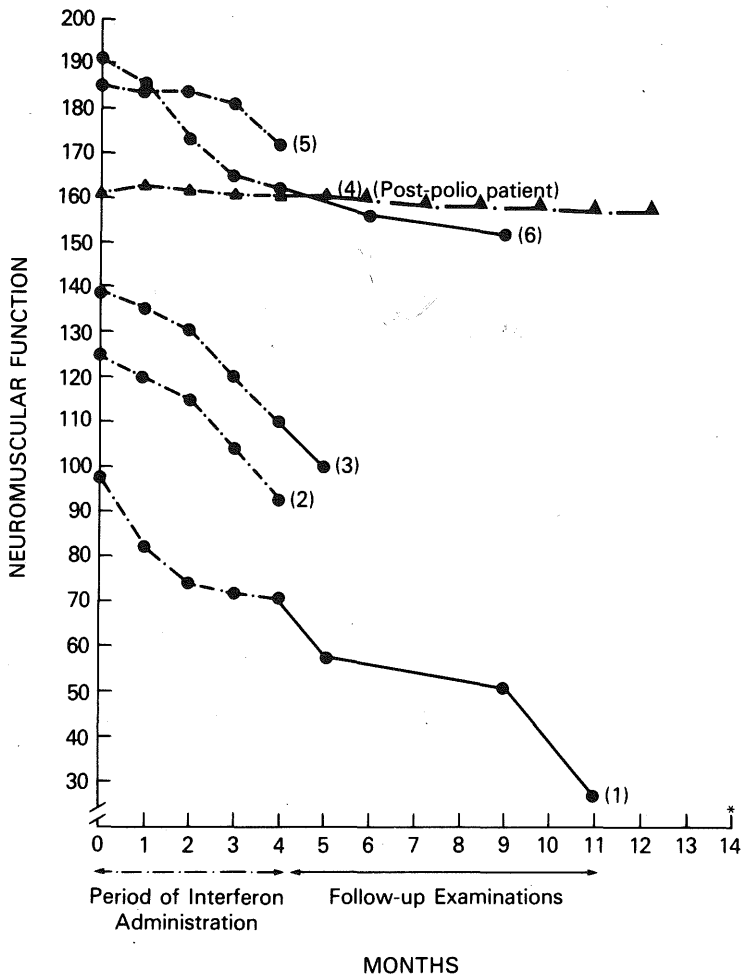


Fig. 2. Course of 5 patients (Nos. 1, 2, 3, 5, 6, in parentheses) with ALS and one patient (No. 4) with PPMA during a trial with administration of interferon, as we reported [22]. Total neuromuscular score in this study was the sum of a functional score (normal 60) based on the patient's neuromuscular function and a motor examination score (normal 176) as reported [22]. Asterisk indicates the condition of the patients 14 months after interferon administration. The course of the ALS patient is clearly different from the one with PPMA. All ALS patients substantially worsened during the period of 14 months of observations. At the end of the 14-month period, *Patient 1* became quadriplegic on the respirator; *Patient 2* became quadriplegic and developed bulbar signs; *Patient 3* became quadriplegic, motionless with severe bulbar and respiratory involvement; *Patient 5* became quadriplegic with bulbar involvement; and *Patient 6* developed bulbar signs and needed assistance to ambulate. In contrast, *Patient 4* with PPMA remained essentially unchanged or perhaps only slightly worse.

rarely have we seen occasional ALS patients with lymphocyte subpopulations and immunoregulatory ratio above or below the normal range. This is probably not different from the normal aberrations anticipated in an immunocytochemical assay. In fact, up to 2% to 3% of our normal volunteers could have such irregularities, which may vary according to activity, recent viral illness, common colds, or other undetermined factors (Dalakas, unpublished observations).

Search for antibodies to CNS cell components failed to reveal specific binding to neurons, glial cells, or vascular endothelial cells in any of the patients with ALS or PPMA. Spinal fluid analysis for oligoclonal bands revealed the presence of 2 to 4 IgG bands in up to 50% of PPMA patients [21]. This is in contrast to the CSF of our patients with classic ALS, where no bands have been seen. It is of interest that 5 asymptomatic post-polio patients (2 studied 3 years after the acute infection), did not have oligoclonal bands in their CSF. Whether an antibody IgG response to neuronal (or viral components) is manifested only in some of the post-polio patients who have new weakness (PPMA) is only speculative at the moment. Oligoclonal bands in the CSF, often against known viral proteins, are present in other subacute, chronic, or latent viral diseases of the CNS such as subacute sclerosing panencephalitis (SSPE), herpes, progressive multifocal leukoencephalopathy (PML), or AIDS encephalopathy [26]. Their presence in PPMA patients who have suffered a viral motor neuron infection many years earlier, and not in patients with ALS who have no history of a known virus infection, could be interpreted to suggest that if ALS is due to a virus, this virus probably behaves differently than the other *conventional* viruses affecting the human CNS.

Muscle Biopsy With Enzyme Histochemistry

The histochemical findings in muscle biopsies of 35 PPMA patients, 5 asymptomatic post-polio patients, and 27 ALS patients are summarized in Table 1. The main histologic findings in PPMA muscles compared to ALS muscles include:

Large fiber type grouping of normal size fibers. These groupings, containing up to 170 muscle fibers per group, are present in all PPMA muscles. This suggests that in PPMA, the surviving motor neurons have overcompensated for the lost ones by excessive oversprouting of their distal axons in an effort to fully reinnervate and control a larger than normal area of muscle function, resulting in motor unit sizes of giant proportions. In ALS, on the other hand, the fiber type grouping of normal size fibers is usually slight, is present only in 25% of the biopsies, and contains not more than 25 muscle fibers per group (Figs. 3a and b). This suggests that in ALS, the degree of compensation via axonal sprouting is incomplete, due to either impaired sprouting and reinnervation or the shorter life-span of motor neurons.

TABLE 1. Differences in the Muscle Biopsies of Patients With ALS and PPMA

	PPMA	ALS
Fiber type grouping of normal size fibers	always present even in asymptomatic muscles (up to 170 fibers per group)	found in up to 25% of the patients (groups are <i>much smaller</i> than those noted in PPMA)
Scattered angulated fibers	present in PPMA (absent in asymptomatic post-polio)	present
Group atrophy	not found in the <i>newly</i> weakening muscles	always present in the weakening muscles
Inflammation	up to 40% of biopsies	rare
Hypertrophic moth-eaten and targetoid fibers	often present due to long-standing partial denervation	rare

Scattered angulated fibers and group atrophy. Angulated fibers, scattered among the normal size fibers, are always found in PPMA (Fig. 4a) as well as in ALS, but not in the asymptomatic post-polio muscles [5, 21]. Group atrophy, however, present only in ALS (Fig. 4b), is characteristically absent in PPMA [3, 21], although small group atrophy can theoretically develop [27]. This indicates that in PPMA, the ongoing compensation with excessive distal sprouting and motor unit enlargement stresses the neuronal cell body, which after a number of years can neither support further reinnervation nor meet the metabolic demands of all the distal sprouting. This results in slow disintegration of some nerve terminals (represented as small, scattered, angulated fibers) but not death of the whole motor neuron. In contrast, if major axonal branches or entire neurons were progressively dying, as in ALS, atrophic fibers in groups (group atrophy) would have developed, resulting in more severe and rapidly progressive muscle weakness.

Perivascular or interstitial inflammation. This consists predominantly of lymphocytes and is present in up to 40% of the PPMA biopsies [5, 21]. Inflammation is seen only rarely in ALS and other motor neuron diseases, but it can be seen occasionally in neuropathies. Such inflammation, especially in areas unrelated to fiber necrosis, could represent an ongoing disease activity similar to the presence of mild inflammation we have seen in the spinal cord of PPMA patients [18]. The possibility cannot be excluded that in PPMA, these lymphocytes represent an ongoing immune response in a form of activated lymphocytes, similar to those seen in other autoimmune neuromuscular diseases such as myasthenia gravis.

Hypertrophic fibers with internal nuclei, "moth-eaten" and targetoid fibers. These common findings in the muscles of PPMA patients are rare in ALS [5, 21]. They represent an effect of a chronic denervating state, possible overuse, or an attempt of the muscle fiber to adapt to increasing work

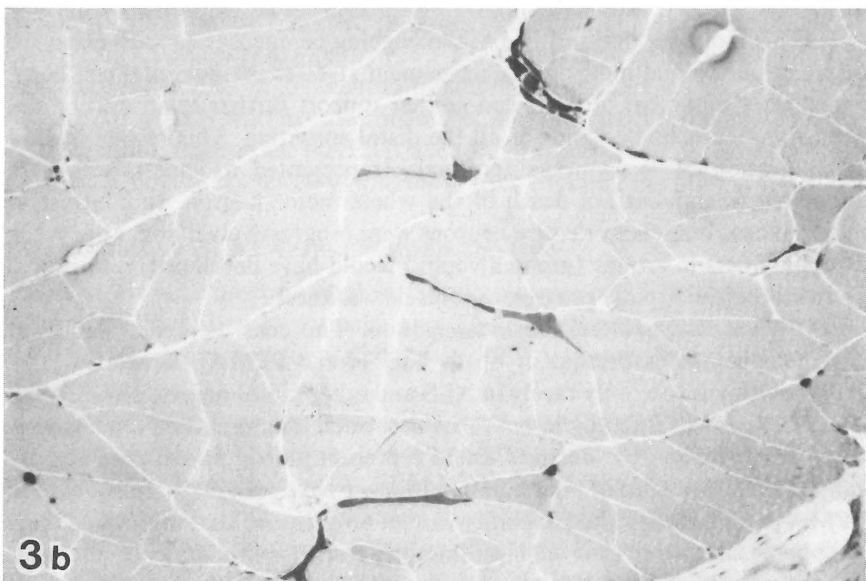
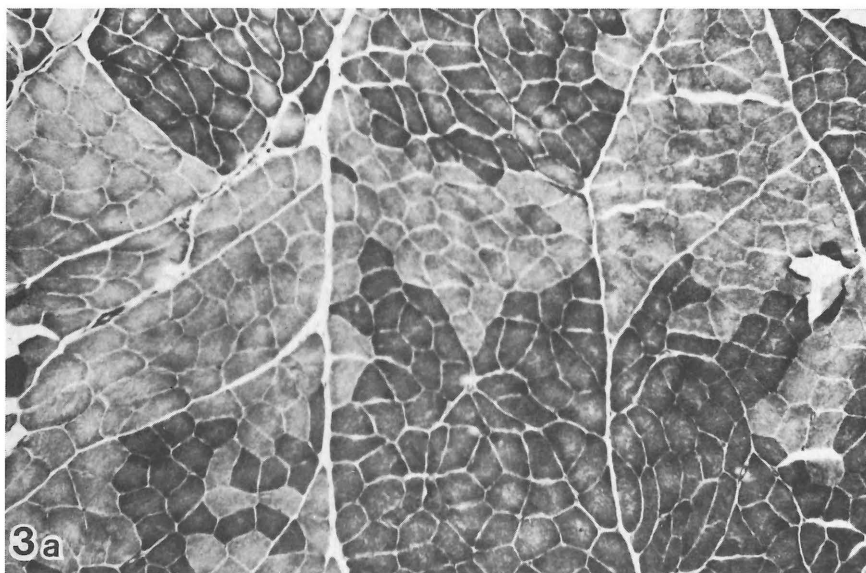


Fig. 3. Muscle biopsies from patient with PPMA (a) and ALS (b) stained with ATPase. Large groups of both fiber types are noted in PPMA while very small groups are noted in ALS. Both biopsies are from muscles with relatively normal strength.

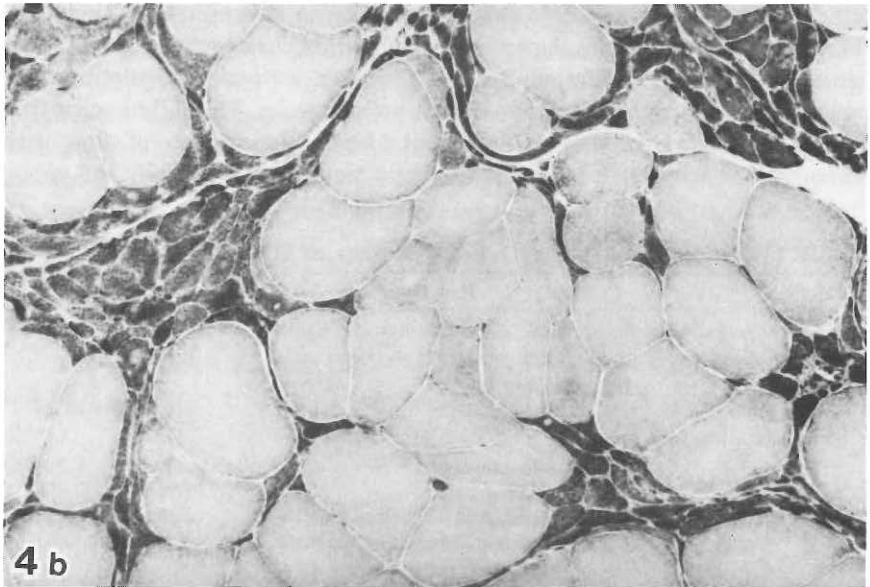
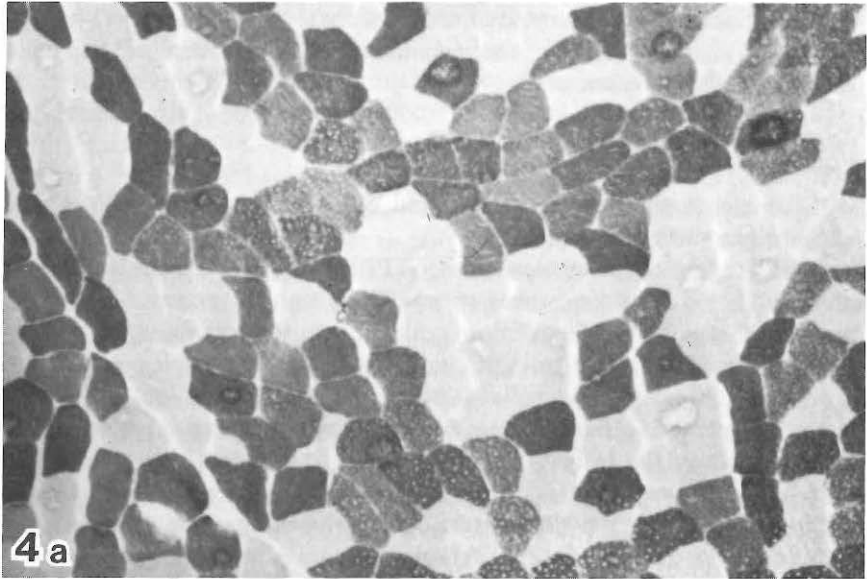


Fig. 4. Biopsies from newly weakened muscles from a patient with PPMA (a) and ALS (b) stained with nonspecific esterase. Small, scattered angulated fibers, the hallmark in PPMA, are prominent in (a) with one very small area of group atrophy containing 4 muscle fibers. In contrast, in ALS (b) there is severe group atrophy.

demands. Such fibers are very rare in ALS, probably due to the short life-span of the disease and underuse of the remaining muscles as a result of the rapid progression of the weakness.

Electromyographic Findings

The electrophysiologic findings and differences between PPMA and ALS are summarized in Table 2.

With regard to spontaneous activity, PPMA muscles demonstrate fibrillations and positive sharp waves (psw). These signs of active denervation, however, although more frequent in weakening muscles, can also be found in what appears to be "stable" muscles. They can be found in stable muscles even 3, 5, 15, or 20 years after polio. It should be emphasized that a "stable" post-polio muscle is a relative term because stability is very subjective when the clinician sees the patient for the first time. In addition, since the patient often focuses his or her attention on the weakest area, contiguous or remote muscle groups that may have started to worsen may be unnoticeable. Therefore, whether a fibrillating "stable" muscle is indeed "stable," or has started to weaken without the patient's awareness, is uncertain. Only follow-up examination can elucidate this, and caution in interpretation is advised. For comparative purposes, however, it is clear that the degree of spontaneous activity, including fibrillation, positive sharp waves, and fasciculations, are much more frequent in ALS than in post-polio muscles. This difference is true not only in the frequency of firing but also in the number of sites with abnormal activity. In practice, this distinction is of no significant value,

TABLE 2. Electrophysiologic Findings in Post-Polio State and ALS

	Post-Polio*	ALS
Fibrillations and psw	present (+); stable muscles (\pm)	+++
Fasciculations	frequently present (+) (rare in stable muscles)	+++
Giant, potentials, of long duration, polyphasic	often above 10 mv	rarely above 10 mv
Fiber density	very high	increased
Jitter and blocking	increased, even in "stable" muscles suggestive of ongoing reinnervation (very unstable in weak muscles)	often increased
Neurogenic jitter	not often seen, suggestive of instability of distal sprouts and failure of reinnervation of groups	often found

*No significant differences were found between PPMA and stable post-polio muscles [17].

+ to +++ refers to the severity of the activity.

however, because it is the *presence* of spontaneous activity that is of diagnostic value, not the *amount* of spontaneous activity.

Perhaps a more meaningful quantitative difference between PPMA and ALS is in the size of the voluntary motor unit action potentials and in the fiber density and degree of blocking (Table 2). All 3 of these parameters are increased in ALS, but have reached giant proportions in PPMA. For example, the amplitude of reinnervating voluntary motor unit polyphasic potentials is rarely above 10 mv in ALS, but usually above 10 mv (often 15–25 mv) in PPMA muscles. The same is true for the fiber density. These observations are consistent with the size of fiber type grouping we noted in the muscle biopsies and indicate that in PPMA, the motor neurons have been excessively stressed to reinnervate, resulting in giant-size motor units. In ALS, on the other hand, the process is limited either because the motor neurons do not live long enough for their reinnervating process to reach functional maturity or because their capacity to oversprout is impaired by sickness of the cell. Increased jitter and blocking found in stable and PPMA muscles suggest an ongoing reinnervating process, as initially proposed by Wiechers and Hubbell [28] and confirmed by us [3]. These findings are also found in ALS and no clear quantitative difference between the two conditions exists.

“Neurogenic jitter,” characterized by a synchronous variation of at least 2 muscle fibers that jitter together with respect to a third, can be found often in ALS [29] but not in PPMA [3, 17, 28]. This suggests that in PPMA, newly regenerated axons show instability at the points of the axon branches, resulting in failure of further reinnervation of groups because the cell body has reached its maximum capacity for regeneration and can no longer maintain the most distal sprouts. This finding is also supported by the small scattered angulated fibers found in the muscle biopsy and the absence of new atrophic fibers forming groups [3].

Spinal Cord Examination

The pathologic findings of the spinal cord in stable post-polio, PPMA, and ALS are summarized in Table 3. The most striking finding in post-polio

TABLE 3. Spinal Cord Examination in Post-Polio State and ALS

	PPMA or Stable Post-Polio	ALS
Inflammation	yes, perivascular and in the parenchyma of the gray matter	absent
Active gliosis	yes, disproportional to the neuronal loss	gliosis, proportional to the neuronal loss
Neuronal atrophy	present, with chromatolysis	chromatolysis rare
Axonal spheroids	yes	only in rapidly progressive ALS
C-S tracts	spared	always affected

was the presence of inflammation that we found even up to 44 years following the acute infection [18]. The inflammation was both perivascular and parenchymal in the gray matter, with active gliosis disproportional to the neuronal loss. The surviving neurons, present throughout the gray matter, had an abnormal configuration of their soma, whereas others were in the chromatolytic state. In contrast, ALS spinal cords show no inflammation, the gliosis is proportional to the loss of neurons, and no chromatolysis is present. Degeneration of the corticospinal tracts, almost always present in ALS, was not found in our post-polio patients. Another interesting observation was the presence of axonal spheroids in 3 PPMA patients. Axonal spheroids are found in rapidly progressive ALS [30] and represent a defect in the transport of neuronal material from the neuron down the axon, similar to the axonal swellings seen in IDPN intoxication [31]. Axonal spheroids are only rarely seen in conventional ALS. Their presence in PPMA neurons supports our view that these neurons in PPMA cannot maintain the metabolic needs of their distal axons with a possible defect in the axonal transport.

Metabolic Status of Cortical Neurons

The cortical metabolic activity of the ALS and PPMA cortex was studied with the PET scan using ^{18}F -2-deoxy-D-glucose [19, 26]. In PPMA and ALS patients with disease confined to lower motor neurons, the metabolic activity of the cortex was normal. In contrast, in patients with advanced ALS and upper motor neuron involvement, there was a diffuse hypometabolism, averaging 22% below normal, throughout the cortex and basal ganglia but not the cerebellum. The degree of hypometabolism in ALS patients correlated with the length of disease. The difference between ALS and PPMA in the metabolic activity of the cortex adds another dimension to the differences described above between these two motor neuron diseases.

DISCUSSION

All the above-described differences indicate that PPMA is not and does not lead to ALS. A benign, very slowly progressive motor neuron disease confined to lower motor neurons; PPMA has more differences than similarities to ALS. Confusing the two, therefore, should be avoided, and if clusters of PPMA patients are reported as having "ALS," such a report should be investigated cautiously. At the present time, a post-polio patient appears to have the same chance of developing ALS as the non-post-polio sufferer. An ongoing epidemiologic survey that is now being conducted by the Center for Health Statistics (Dalakas, personal communication, 1986) should substantiate (or disprove) our contention.

Some points need further clarification. We have seen and heard of very

rare post-polio patients who died with respiratory muscle weakness in a fashion resembling ALS. This can happen to a post-polio survivor who has been left with a severe residual respiratory muscle deficit from the original polio compounded by such new factors as: 1) congestive heart failure and other medical problems compromising respiratory reserves, intrinsic lung disease (ie, emphysema) or frequent bronchopneumonias; 2) PPMA predominantly affecting the thoracic motor neurons, diminishing further the already compromised respiratory muscle reserves.

If PPMA affecting the respiratory muscles does develop, it should progress slowly enough to enable monitoring with pulmonary function studies. The mechanism of PPMA predominantly affecting the thoracic muscles is identical to the mechanisms proposed for the PPMA affecting the limbs [3]. It should be remembered, however, that the manifestation of new respiratory muscle weakness in PPMA depends on the patient's condition at the "starting point"; respiratory muscles can be weakened only in those patients who have minimal thoracic muscle reserves, not in those PPMA patients who, at their "starting point," had only limb weakness and adequate-to-normal respiratory function.

We have heard from colleagues that rare post-polio patients develop spasticity. Three such cases were recently reported [32]. In my approach to evaluation of such a patient, I ask the following questions: 1) Were other causes of spasticity producing upper motor neuron disease ruled out? 2) Is there significant scoliosis, not uncommon in post-polio patients, compressing the spinal cord? 3) Has magnetic resonance imaging or myelogram been performed to rule out other concomitant spinal cord disease?

If everything else has been ruled out, and the patient has spasticity and new muscle weakness with diffuse atrophy and fasciculations, the possibility of ALS should be considered, not because it is more common in post-polio, but simply because post-polio patients are not immune to developing ALS. Occasionally, positive Babinskis can be seen in PPMA patients [33]. If no other upper motor neuron signs are present, this finding is of uncertain significance. It probably represents dysfunctions of cortical neurons that were also clinically or subclinically affected during the original illness in a form of polio-meningoencephalitis.

From the comparative analysis of the clinical, histologic, electrophysiologic, metabolic, and histochemical findings, we can make some speculations regarding the neurobiology of motor neuron diseases. After a viral insult to the motor neurons (acute polio), there appears to be evidence of ongoing activity, with a continuous effort of the surviving motor neurons to reinnervate and remodel their motor units. Evidence of such a continuous activity was based predominantly on our electrophysiologic findings of denervation/reinnervation even in stable post-polio muscles 5 to 10 years after polio (Huang, Hallett,

Dalakas, unpublished observations) and was supported by one recent case, 2 years after vaccine-associated polio [34]. It appears, therefore, that the motor neuron remodeling is different than in a static nerve injury, where stability occurs a few months after reinnervation [35]. The presence of continuous activity in post-polio is also supported by our observations in the spinal cord, where we have found active gliosis and inflammation many years later, raising the possibility of a smoldering neuronal dysfunction, which, although subsided, did not completely cease after the acute infection.

PPMA appears to develop in some patients an average of 30 years after the original polio attack [1–4, 21]. Based on our analysis of these patients' muscle biopsies and EMG findings, it appears that motor neurons that have been stressed to maintain enlarged motor units for a long time cannot maintain the metabolic needs of their distal axons, resulting in disintegration of some distal sprouts. Is the 30-year period of overfunctioning the time limit for those neurons, after which dysfunction begins? Unfortunately, no information exists in a human biologic system to provide information regarding the life-span of a hyperfunctioning neuron. If spinal cord neurons start to decline in function after the age of 60 due to the process of aging [36], we may be able to speculate that in PPMA, there may be a premature aging process and that these neurons succumb to attrition faster than normal. Future studies using experimental models should give us such information regarding the viability of a neuron that has been stressed to oversprout and control a larger than normal area of motor function.

From the PET scan studies, it is evident that ALS is a more generalized disorder extending beyond the corticospinal tract and the motor cortex. It also appears that motor neuron diseases confined to lower motor neurons, such as PPMA, have intact cortical metabolism. This suggests that the functional integrity of the upper motor neuron does not depend on a signal from its lower motor neuron target via the corticospinal tract, and it differs from the behavior of the lower motor neurons, which disintegrate after their peripheral axon is cut [37].

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DISCUSSION

DR. JUBELT: I just want to comment briefly about the upper motor neuron findings. We have seen several post-polio patients who had upper motor neuron findings manifested as increased reflexes or Babinski sign, and I would say it is found in less than 5% of the patients. From experimental studies, it is clear that the polio virus can infect upper motor neurons. If you look at the literature on human poliomyelitis, you will find upper motor neuron findings described in some patients early in their course of polio. Now, I don't know why I have seen a few of these and you haven't. I was talking to Dr. Mulder earlier and it may well be that some of the patients that we see are actually referred with the question, do they have ALS? Usually these patients have a very slow course, their EMG does not look like ALS with a lot of denervation, even though if you looked at them at one point in time, they have both upper and lower motor neuron signs and no evidence of cord compression on MRI or myelographic studies.

DR. DALAKAS: I agree with your speculation that these patients' upper motor neuron signs may be due to possible involvement of the upper motor neurons during the original illness. We did not find upper motor neuron signs in the 60 patients or more that we have examined, but our patients didn't really come to see me in order to rule out ALS. Perhaps, it is a sampling, but an occasional

isolated upper motor neuron sign, ie, Babinski, with negative work-up for myelopathy and normal reflexes is of uncertain significance. Only long-term follow-up could clarify this.

DR. MULDER: We did have some patients in our original series who had upgoing toes. They were referred to us as ALS. We had problems evaluating those patients because so many of them had had very serious illness as well as multiple surgical procedures on their legs and feet. I guess it would be very hard to sort out when the upgoing toe was meaningful or when it was just because of unusual musculature, and I presume we were not completely certain about that when we finished. I would think it is perfectly possible that some patients could have two diseases or surely patients that we saw early on had involvement of the cerebrum in addition to the anterior horn cells.

DR. ANTEL: Your observations about the spinal fluid immunoglobulin raise a number of complicated questions. Once an animal or a human has an acute viral encephalitis and there is an initial immune response, does that individual retain evidence of that indefinitely? I think the prototype for this is probably a mumps meningeal encephalitis. What is known, if at all, about acute polio, and have you had a chance to look at the spinal fluid in terms of an immune response, and does that persist indefinitely? I think that is important in terms of the questions that are raised about second infections or postviral syndrome superimposed on polio as to whether this is really a new immune response or not. Perhaps I could ask Burk Jubelt to comment. Burk, in animal models with your viral encephalitis or others that Diane Griffin and your colleagues have worked with, once an immune response is seen, especially an immunoglobulin response or clonal bands, does that ever disappear?

DR. JUBELT: In the animals it seems to persist in the spinal fluid and in the nervous system over a long period of time. Obviously this hasn't been looked at in detail in humans, but at least in the animal models it seems to persist.

DR. DALAKAS: Jack, you are really raising a very important question and one that we have been trying to answer. I am desperately looking for patients with acute polio and, as you know, it is very difficult, almost impossible, to get acute polio patients in this country. We did manage to get spinal fluids from Dr. Huang from Taiwan where there was a recent epidemic. These spinal fluids were from patients who had acute polio 2 to 3 years ago and their CSF was negative for banding. This was not fresh spinal fluid, however, because it travelled from Taiwan for several days at room temperature. I do not, therefore, know if these bands were not detached due to poor preservation of the CSF or they have actually disappeared.

DR. JUBELT: Marinos, have you looked to see if the banding that you did find in these patients is directed against polio virus antigens at all?

DR. DALAKAS: We are trying to do that now.

Post-Polio Syndrome and Amyotrophic Lateral Sclerosis: A Relationship More Apparent Than Real

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A relationship between preceding acute anterior poliomyelitis and development of motor neuron disease occasionally has been suggested since first postulated by Charcot in 1875, during his discussion of a case report by Raymond [1]. That patient had left-sided weakness and hemiatrophy following a febrile disease at age 6 months, and when he was age 17, he developed progressive wasting, weakness and fasciculations of the previously uninvolved right arm and leg. Subsequently, in 1903, Potts reported a similar case and reviewed 35 other reported cases [2]. Of these, 28 had a disease that seemed to resemble progressive muscular atrophy, 2 resembled amyotrophic lateral sclerosis (ALS) because they had upper and lower motor neuron signs, and 2 had myelitis with sensory involvement. In an additional 4 cases, the patients possibly had a second attack of acute anterior poliomyelitis. Subsequent reviews of this situation appeared in 1935 by Salmon and Riley [3] and in 1952 by Geyer [4]. In 1962, Zilkha [5] recorded an additional 11 cases, making a total of 83 documented instances of the supposed relationship of post-polio syndrome (PPS) to motor neuron disease.

The striking feature of PPS that emerged even from the earlier cases was that the acute poliomyelitis seemed to occur within the first 5 years of life with only a few exceptions. Two exceptions quoted by Geyer [4] were aged 32 and 15 when they had poliomyelitis, and in a review by Campbell in 1969 [6], a patient had polio at age 21.

The second finding that emerged, which was emphasized by Zilkha in 1962 [5] and by Campbell in 1969 [6], was the relatively benign nature of PPS compared to ALS, with slow progression being the rule in PPS and rapid progression characterizing ALS. Another point also made by Campbell and Zilkha was the paucity of upper motor neuron signs in the PPS, even after 2 years of observation, while upper motor neuron signs are quite common in ALS. Zilkha emphasized, but Campbell does not seem to mention, that

fasciculations of the tongue are not as ominous a sign in patients with PPS as they are in ALS patients [5]. Usually fasciculations of the tongue in ALS would indicate involvement of the hypoglossal nucleus and would predict bulbar involvement. This would then be a poor prognostic sign because of imminent difficulty with management of secretions, swallowing, talking, and respiratory control. Muller in 1952 [7] had reached similar conclusions related to the slow progression of PPS, the lack of upper motor neuron signs, and the benign nature of tongue fasciculations in his review of cases in Sweden.

In 1972, Mulder, Rosenbaum, and Layton [8] published their now classic paper, "Late progression of poliomyelitis or forme fruste amyotrophic lateral sclerosis?" Their study, based on 34 patients seen at the Mayo Clinic between 1942 and 1970, had the advantage that all of the patients were actually examined by at least one of the authors. The patients included in that study met strict criteria, including a credible history of poliomyelitis, a partial recovery of function, a minimal 10-year stabilization period, and the subsequent development of progressive muscular weakness. Verification of the original diagnosis of poliomyelitis was established in their patients by discussion with the patient and relatives and the study of old hospital records. Twenty-five of the 34 patients had muscle fasciculations, 4 had Babinski sign, and 2 had equivocal evidence of a Babinski sign. No significant sensory abnormalities or extrapyramidal signs were noted. Twenty-seven of the 34 had been examined with electromyography (EMG), and fasciculations were found in 25 of those 27 patients. EMG studies showed evidence of neurogenic atrophy with reduced numbers of motor unit potentials, increased amplitude, increased duration of motor unit potentials, and an increased proportion of polyphasic motor unit potentials. Their conclusion was that many of their patients were diagnosed as having ALS but that the clinical examination of these patients indicated that they probably did not have ALS. The major difference that emerged from their analyses of their cases was that PPS differed from ALS in prognosis. From their experience, ALS patients died an average of 3 years from the onset of first weakness, but in their group of patients studied for an average of 12 years since onset, only 4 had died, and 3 had died from causes unrelated to muscle weakness. Thus, it was apparent from their study that patients who develop PPS, even though their disorder bears a superficial resemblance to ALS, live longer, and progress more slowly than those with real ALS. Mulder et al [8] also claim that the syndrome can be distinguished from ALS because of the lack of lateral column signs in PPS, whereas such signs are common in ALS. This conclusion is probably not justified by their data, since they did not have 6 patients with Babinski signs and it had been previously reported that Babinski signs do occur in PPS. For

instance, 5 of Zilkha's 11 patients had extensor plantar responses on one or both sides [5].

That more or less brings us to the modern era of clinical investigations using sophisticated laboratory data and the classic paper of Dalakas et al [9], with which all true students of the PPS are familiar. Briefly stated, Dalakas has shown, in the study of 27 patients in whom new muscle weakness developed after recovery from acute polio, that the rate of progression was on the average 1%/year. The decrease was irregular, with subjective plateau periods that ranged from 1 to 10 years; and none of those patients had clinical or laboratory evidence of ALS. Interestingly, oligoclonal bands were found in the cerebrospinal fluid (CSF) of 7/13 patients studied, and inflammatory changes were present in 12/27 biopsy specimens. The conclusion was that new post-polio muscle weakness is a relatively benign form of motor neuron deterioration. The weakness is not due to a loss of whole motor neurons, as in ALS, but rather to a dysfunction of surviving motor neurons that causes a slow disintegration of the terminals of individual nerve axons. Their actual conclusion was never really justified by the data presented since they did not directly demonstrate disintegrating axons and preserved neurons. Other people who have done muscle biopsies on patients with PPS, ourselves included, have found grouped small atrophic fibers that are identical to those seen in ALS, indicating that whole motor neuron degeneration can occur in PPS.

The conclusion that we have reached from our review of the previous papers on this subject is that PPS and ALS are clinically similar diseases that are probably not related to each other. The similarities are quite apparent, in view of the asymmetric weakness accompanied by fasciculation and atrophy that begins insidiously in middle life and is gradually progressive. The absence of sensory findings and other evidence of widespread nervous system disease is also characteristic of both conditions. Furthermore, EMGs reveal fasciculations and fibrillations in both conditions and relatively normal conduction velocities. Muscle biopsies are almost identical in both conditions. Our detailed study of the muscle biopsies in ALS has been reported previously and subjected to the same computerized analysis that we report here for the PPS [10]. Therefore, clinically it would appear that these 2 illnesses can be differentiated only on the basis of minimal evidence of lateral column involvement in PPS and maximal evidence of lateral column involvement in ALS; some patients with PPS, however, show evidence of lateral column involvement by exhibiting Babinski signs. The major distinguishing feature between the 2 conditions is obviously the rate of progression; PPS is a much more benign disorder.

Previous retrospective epidemiologic studies of the frequency of preced-

ing poliomyelitis in ALS have reported a statistically significant increase in the expected prevalence of ALS among such patients [11]. Poskanzer et al [11] suggested that although 0.6 patients might be expected by chance alone to have had previous poliomyelitis among the 196 with ALS that they reported, the true prevalence was 5. The difference between the expected and the actual prevalence was considered to be highly significant ($P < 0.001$). In the retrospective case-controlled epidemiologic study done by Pierce-Ruhland and Patten [12], there also was an increased prevalence in ALS patients who had a history of polio. In that study, 88 ALS patients were age- and sex-matched to control patients who had lived in the same childhood environment. Five of the 88 ALS patients and none of the controls reported a history of acute poliomyelitis or anything very similar to it that led to paralysis in childhood and subsequent recovery with residual weakness. We were unable, of course, to examine the data on the individual patients reported by Poskanzer et al [11], but we were able to review the cases reported in our original epidemiologic study [12]. We now feel that the 5 patients whom we considered to have ALS associated with poliomyelitis were actually cases of PPS and, in retrospect, we would not have classified them as having ALS. Probably some of the other studies that showed increased occurrence of polio in the childhood histories of patients with ALS have simply misdiagnosed the ALS and should have diagnosed PPS instead. We made that mistake and others might be making the same error. The epidemiologic studies indicate the truth of Harley's famous statement. "The past is another country; they do things differently there." Had we been able to go back and redo our epidemiologic study and our subsequent published report, we would not have included those patients with polio. Therefore, we would have ended up with a series of no ALS patients with a previous history of polio, no controls, and no statistically significant increase of a history of poliomyelitis among ALS patients!

CASE STUDIES OF SEVERE POST-POLIO SYNDROME

METHODS

Patient Selection

All patients, studied after giving informed consent, had a history of acute paralytic poliomyelitis or something very similar to polio in childhood or in adolescence. This was established by an interview with the patient, a careful review of records to document as well as possible the clinical occurrence of acute febrile illness followed by paralysis, and in most cases, by review of childhood pictures that illustrated the patient's muscle weakness and atrophy in the affected limbs. All patients were referred to Dr. Patten as private

patients for evaluation of severe progressive muscle symptoms occurring in later life. The patients enrolled in this study fulfilled the following criteria: They had partial recovery of motor function after a childhood episode of acute illness resembling polio and functional stability or recovery for at least 15 years; they had residual atrophy, weakness, and areflexia in at least one limb, but with relatively normal or preserved sensation; and they had new muscle weakness in a limb unrelated to the limb that had the previous muscle atrophy and weakness.

Neuromuscular Evaluation

All patients were given neurologic evaluations by Dr. Patten and several other neurologists. They were all followed by one neurologist, Dr. Patten. Specific attention was paid to neuromuscular function and quantification of the patient's muscle strength in relationship to gripometer readings. A force gripometer was used for every patient. The gripometer was the one used in our practice over the last 13 years. Each patient was asked to show a maximum grip strength on both the right and left side, and this number was recorded in the chart for each clinic visit. In addition, the patients were asked to lie on their backs while we elevated their legs at a 45° angle, and then hold their legs at that angle for as long as possible. When the legs began to drop below the 45° angle, a stopwatch was stopped and that number was recorded as the number of seconds that the patients were able to hold their legs against gravity. In the same way, the patients' heads were lifted off the bed and they were asked to hold their heads there as long as possible. When the head fell back to the bed, a stopwatch was clicked and that number was recorded as the head-holding time. Those patients who were able to hold their heads against gravity for 60 seconds or more were told to stop and the number 60 was recorded in the chart as the normal value. The Medical Research Council scale was not used to evaluate the patient's strength because it is not quantitative, not linear, and relatively useless in the appraisal of small changes in muscle strength.

Laboratory Studies

Each patient had a multitude of blood and urine studies, a spinal tap, a muscle biopsy, and in many cases, a nerve biopsy. Electromyograms with nerve conduction, needle electromyography, and repetitive stimulation studies were done on each patient.

Statistical Analysis

Statistical analysis was done using program SPSS PC+ [13], which compared variables with one another and calculated correlation coefficients and probability values for each correlation. This was the same statistical analysis that had been used in our study of the histologic findings in motor

TABLE 1. Summary of Laboratory Items That Should Be Done in PPMABlood testsCBC, ESR, NaKCO₂C1, SMA-15 (should include calcium and phosphate)

T3, T4, TSH and other thyroid tests

Parathyroid hormone level

Blood lead, mercury, aluminum

Rheumatoid factor, antinuclear antibodies, complement levels, serum electrophoresis with high resolution and personal inspection of the plate for monoclonal gammopathy

Hexosaminidase A and B

Serum amino acid screen

CPK

Antiachetylcholine receptor antibody titer

Hepatitis screen for hepatitis surface antigen

Tissue biopsies

Muscle biopsy

Sural nerve biopsy

Biopsies of minor salivary glands if Sjogren is suspected

Other tests

Magnetic resonance of brain and spinal cord

Spinal tap with studies for electrophoresis and oligoclonal bands

Electromyogram looking for decrements with stimulation at low (2 Hz) rates

neuron disease [10]. A detailed explanation of methodology can be found in that paper [10]. Briefly stated, we used standard methods to prepare transverse microscopic sections of fresh frozen muscle cut by a cryostat at 10 μ thickness and used the ATPase activity at pH 9.4 to ascertain fiber type. After photographing etched micron standards and the central parts of the biopsy specimens, we were able to measure directly from the photograph the smallest fibers that were present, and any fiber below 12.5 μ was considered a small angular fiber. Using this technique, we calculated histologic variables, including type 1 grouping, which was the maximum number of contiguous type 1 fibers in the ATPase stained sections, providing that a contiguous fiber touched 2 or more fibers of its own fiber type. Type 2 grouping was the maximum number of contiguous type 2 fibers in the ATPase stained sections of pH 9.4. Grouped atrophy was considered the maximum number of contiguous atrophic fibers in the diphosphopyridine nucleotide dehydrogenase tetrazolium-reductase stained sections provided that an atrophic fiber had a fiber diameter of less than 12.5 μ and stained excessively dark (darker than a type 2 fiber).

From hospital and office records and personal communication with patients and families, we tabulated clinical variables: 1) Age—The patient's age in years at the time of the study (1986); 2) Sex—The patient's statement of sex in a hospital admission record or office admission form; 3) Duration—

The period in years from the onset of symptoms referable to progressive muscle weakness until the time of this report; 4) First—The age in years when acute polio occurred; and 5) SYMPT—The age in years when the first symptom of progressive weakness was detected by the patient.

There were also many other variables, including the initial right hand grip, which was the measured grip strength in pounds on the patient's first visit, and the initial left hand grip. The initial head holding and leg holding times were also recorded as variables, as were the final head and leg holding times, and final grip strengths at the patient's last recorded clinic visit. Computer variables included the rate of progression, for example, the initial grip minus the final grip, divided by the duration of observation. Many other variables were examined, including the incidence of necrotic fibers in muscle biopsies, creatine phosphokinase (CPK) value, lactic dehydrogenase (LDH) value, blood glucose, and multiple hematologic parameters, including the mean corpuscular hemoglobin and mean corpuscular volume. The EMG results included the presence of fibrillations and the nerve conduction velocities. The computer simply identifies a variable by its position in the data matrix and does statistical analysis as designated by the command structure of the program on that variable. The computer program gave descriptive statistics, such as the mean age and duration of follow-up. The large mass of printout data resulted in a number of statistically significant correlations, but in order to avoid talking about correlations that probably have little or no clinical meaning, we arbitrarily selected $P < 0.001$ as the significance level for the correlation among clinical or laboratory variables.

CLINICAL RESULTS

This series consists of 7 patients, 5 men and 2 women. All patients have PPS, as previously defined, with new muscle weakness and muscle atrophy evolving in muscles that had been previously affected and had fully or partially recovered, or evolving in muscles that were clinically unaffected by the original polio.

In all patients, the new weakness was associated with increased muscle atrophy and myalgias. Fasciculations were present in all.

The follow-up period ranged from 1 to 10 years, with an average of 5.6. The mean current age of the patients is 49.3 years with a range of 35 to 68 years. The mean age of new symptoms (that is, the start of PPS) was 38.3 years with a range of 24 to 58 years. The mean age after acute polio when those symptoms began was 33.0 years, with a range of 24 to 58 years. The mean age at which polio occurred was 5.3 years with a range of 1 to 24.

All patients had been weak at some time and had a lower level of functioning because of the weakness. The pace of worsening was usually slow

TABLE 2. Clinical Clues That Suggest Atypical PPS

Exposure to lead
Long-term survival
Exacerbations and improvements
Dry mouth, dry eyes, dry vagina (Sjögren syndrome)
Skin rash, particularly over the elbows, knees, and knuckles
Remarkable worsening with exercise and improvement with rest
Glove and stocking sensory loss to pin and vibration
Other associated diseases of autoimmune origin, particularly severe insulin-dependent diabetes
Diplopia
Enlarged thyroid
Lymphadenopathy
Excessively rapid down-hill course
Positive tensilon test
Poor range of motion of neck (may mean spondylosis)
Ptosis (look for the 'atrophic form of myasthenia gravis')
Excessive weight loss (suggests malabsorption and secondary hyperparathyroidism). Some patients with pancreatic insufficiency have been misdiagnosed as ALS. When there is the slightest doubt, do the appropriate tests to make sure that diagnosis is ruled out.
Diabetes mellitus, especially of recent onset. This is often mistaken for ALS, and these patients have both diabetes and usually an autoimmune inflammatory neuropathy. They should be treated with Cytosan if the nerve biopsy shows vasculitis or inflammation.

except for *Patients CM* and *EM*, who had rapid deteriorations. *Patients GK*, *CF*, and *CM* had evidence of autoimmunity and improved with steroid or immunosuppressant treatment. *EM* recovered with a program of self-improvement. Two others have slowly progressed, and a graph of their progression is seen in Figures 1 and 2.

Four patients had Babinski signs and therefore had signs of upper and lower motor neuron disease simulating ALS. Four patients also had signs referable to dysfunction of musculature supplied by cranial nerves and therefore had bulbar signs.

LABORATORY RESULTS

Five of the 7 (all men) had increased mean corpuscular hemoglobin levels, 5/7 had elevated triglyceride levels, 3 of 7 had increased LDH levels, and 4/7 had increased CPK values. The mean CPK for the whole group was 295.6 μ /liter with a range of 34 to 1,014. The mean corpuscular hemoglobin was 31.7 pg/red cell, with a range of 30 to 33. The mean triglyceride level was 320.4 ng/dl with a range of 255 to 422. Two patients had increased fasting blood sugars above 120 ng. Three patients had decreased serum bicarbonate values below 20 mEq/L and one patient had a bicarbonate above 33 mEq/L. EMGs usually showed diffuse fasciculations, decreased motor units under

Patient #6

Rate of Progression

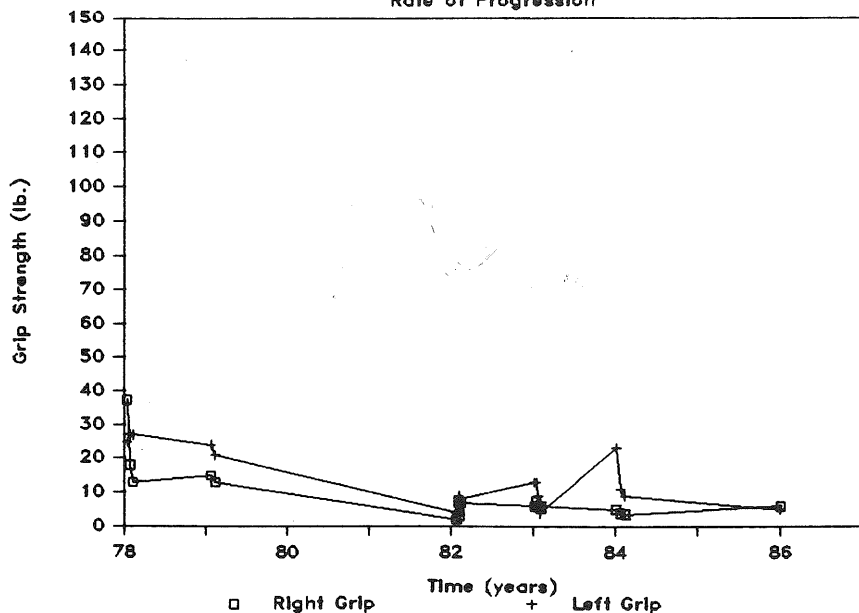


Fig. 1. Right and left grip of *Patient 6* from 1978 to 1986.

Patient #7

Rate of Progression

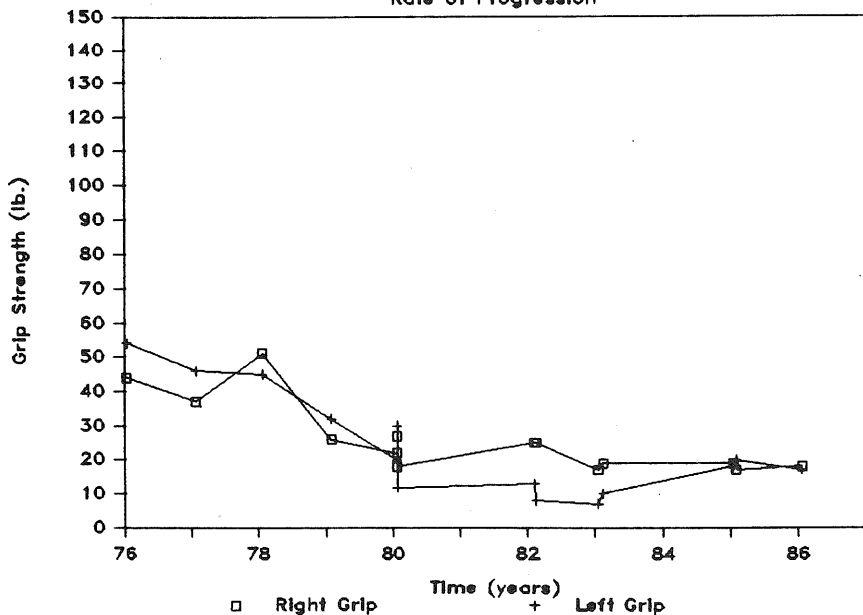


Fig. 2. *Patient 7*, right and left grip from 1976 to 1986.

voluntary control, and normal nerve conduction times. Occasionally, fibrillations were seen. Four of 7 patients had evidence of autoimmunity, including abnormal antibodies, inflammation in tissue, and circulating immune complexes.

Muscle biopsy showed a wide spectrum of abnormalities, including grouped atrophic fibers in 6/7 patients, pyknotic nuclear clumps, and scattered small angular fibers; nerve biopsies showed neuropathy, sometimes with inflammation (Figs. 3–8). In 2 biopsies, oil red O stains were positive for neutral lipid, indicating evidence of neutral lipid accumulation in muscle fibers.

Spinal fluids were all normal, including cell count, protein, sugar, electrophoresis, and percent gamma globulin. All spinal fluids were negative for oligoclonal bands.

STATISTICAL RESULTS

In general, in the same patient, the initial grip, head-holding, and leg-holding times correlated with each other and with subsequent grip, head-holding and leg-holding times. This indicated that the weak, affected neuromuscular system improved as a whole and deteriorated as a whole, and

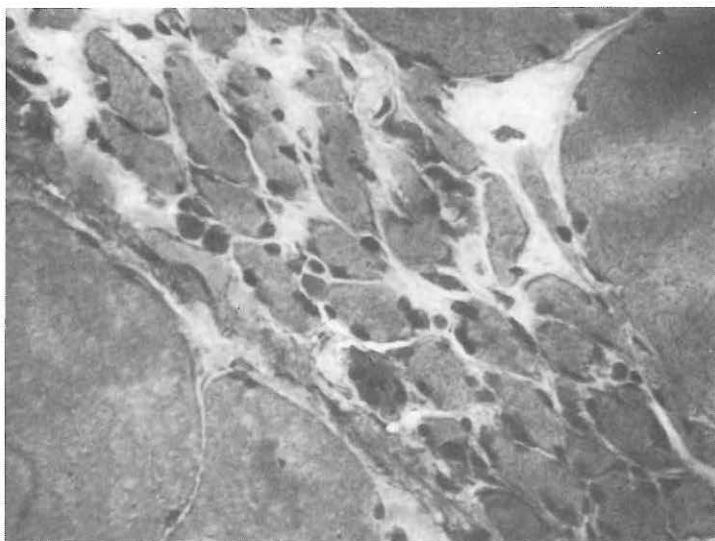


Fig. 3. Modified trichrome on a frozen section of muscle from *Patient CM* ($\times 450$). Note grouped small angular fibers and some pyknotic nuclear clumps.

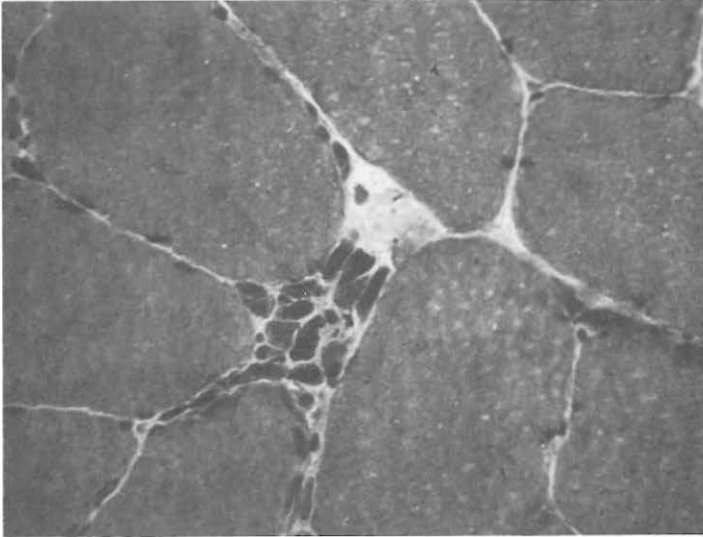


Fig. 4. Modified trichrome on a frozen section from *Patient EM* ($\times 450$). Note group of small angular fibers.

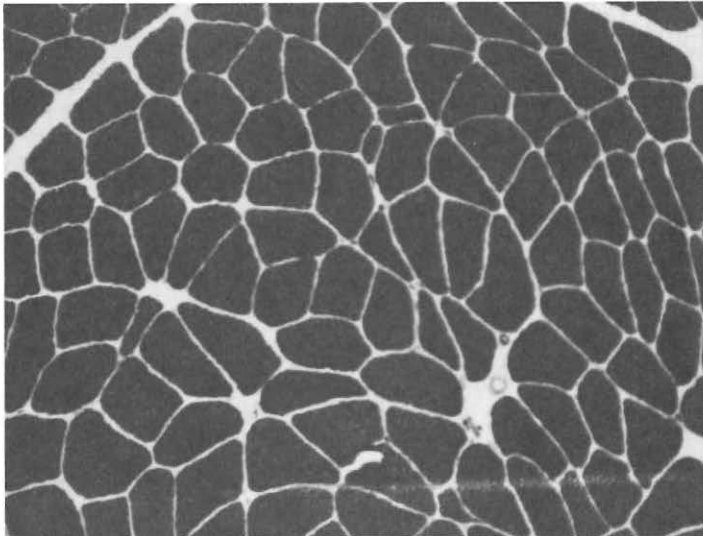


Fig. 5. ATPase at 9.4 from *Patient EM* ($\times 450$). Note type grouping.

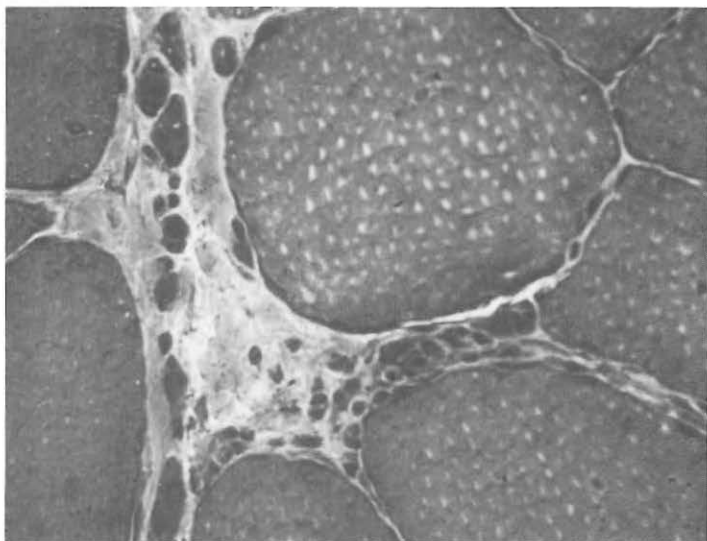


Fig. 6. Modified trichrome on frozen section from *Patient WS*. ($\times 450$). Note grouped small angular fibers.

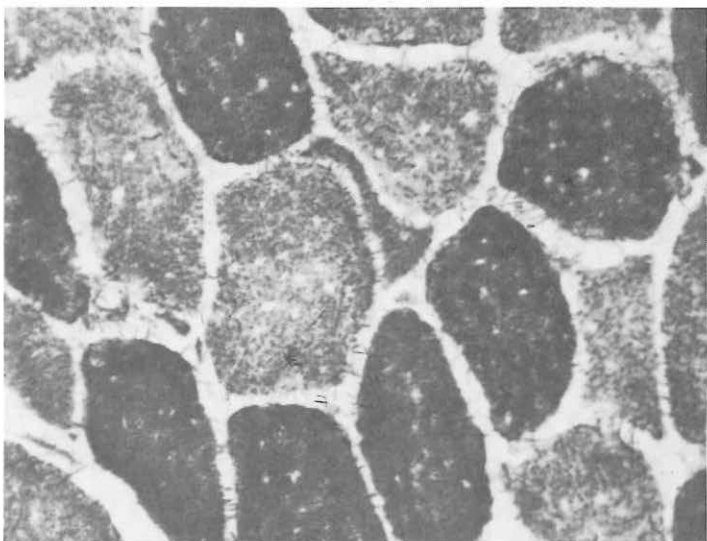


Fig. 7. DPNH-TR stain on frozen section from *Patient SF* ($\times 450$). Note single small angular fiber stained dark indicating neurogenic atrophy. This was the only patient in our series who did not have grouped small angular fibers.

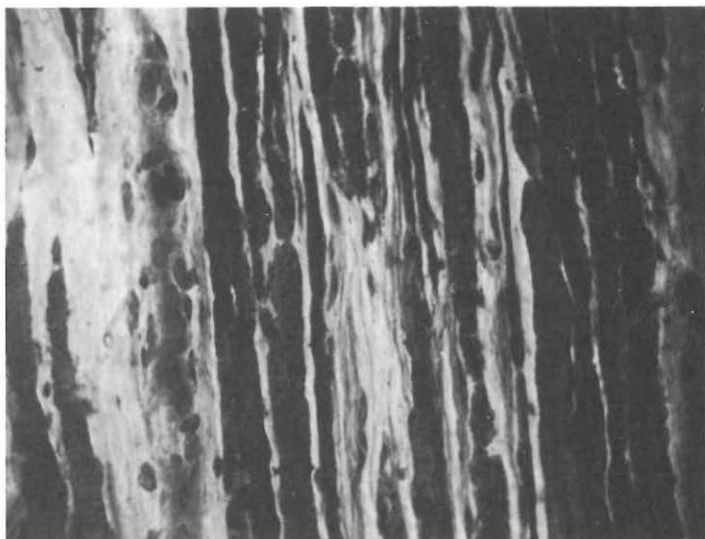


Fig. 8. Modified trichrome on a frozen section of sural nerve biopsy from Patient SF ($\times 450$). Note loss of nerve fibers and increased endoneurial connective tissue.

not just in relation to groups of muscles previously affected by polio. For instance, the rate of deterioration of head holding correlated with high statistical significance with the rate of deterioration of leg holding and with the rate of deterioration of right and left grips. The rate of progression for the group as a whole was -6.4% /year for right grip, -7.2% /year for left grip, -6.7% /year for head holding, and -7.7% /year for leg holding. The average rate of progression was -7.0% /year for all measurements, a value considerably higher than the -1% reported by Dalakas et al [9].

Rate of progression, as measured by grip, leg, and head holding, was not related to any clinical or laboratory variable and specifically did not correlate with age, sex, age of polio, age at first symptoms, atrophy on muscle biopsy, or CPK level. There was a strong inverse correlation between the age of polio and the presence on biopsy of atrophy of type 1 and atrophy of type 2 fibers and with necrotic fibers, indicating that the earlier the polio had occurred, the more likely that those findings would be present on muscle biopsy done at the time that the patient presented to us. The mean corpuscular hemoglobin correlated with male sex, as expected.

DISCUSSION

Our cases differ from those reported by Dalakas et al [9] in several interesting ways that probably reflect the wide spectrum of abnormalities that

can play a role in PPS and the fact that our patients were sicker. Dalakas found that none of 27 patients had ALS; we found none of 7 had ALS, but did find evidence of Babinski signs and bulbar involvement that easily could have led to the misdiagnosis of ALS in those patients. Dalakas found none of 27 patients had grouped small angular fibers; we found that 6/7 did have grouped small angular fibers and neurogenic atrophy every bit as severe as that present in our cases of ALS studied in great detail. Dalakas [9] found 12 of 27 biopsies had occasional small perimysial or perivascular lymphocytic infiltrate, and we found 2/7 patients with the same. Like Dalakas, we found evidence for autoimmunity in several cases. We took that finding one step further and observed significant improvement in 3 patients with treatment. Dalakas observed that slow progression of weakness was the rule, and it probably is, but we note that some patients improved with treatment and one improved dramatically with a program of self-devised social, psychologic, and personal change. Dalakas stated the rate of deterioration was 1%/year; our data showed 7.0% was more likely. Our data were based on real numeric variables and not on the nonlinear MRC scale.

CONCLUSIONS

Post-polio syndrome and ALS are related only by a superficial clinical resemblance and the overlap of neurologic signs in some patients. PPS clearly has a better prognosis, slower progression of weakness, a history of polio, and less evident signs of lateral spinal column dysfunction. Since PPS is a condition about which we really know so little, every patient with this condition must be studied in great detail to try to uncover possible treatable abnormalities and to learn more about the condition. In our experience, autoimmune phenomena are common in PPS and may present opportunities for treatment.

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DISCUSSION

DR. MUNSAT: I think we have 3 different views about the progression of muscle weakness in post-polio syndrome. Dr. Dalakas has reported a 1%/year decline. You have just reported a 7%/year decline in all body muscles, and our data suggest that there is too much noise in the system, too much fluctuation to detect a pattern. One question I think we have to ask ourselves is, “What is the evaluation system we are using?” I would suggest that head holding and leg holding, the MRC scale, and the 100 point scale that Dr. Dalakas uses are neither reproducible or reliable nor are they valid in the sense of measuring what we are trying to determine. I think it is important for us in describing change to define what the reliability of the test is in terms of mean and standard deviation. Now, if a patient loses 7% of baseline strength per year, that means at the end of 7 years, that patient will have lost 50% of muscle strength from the point where he started, and at the end of 10 years it will be 70%. I think that clinical experience doesn’t show that to be the case, so again, I would caution about being careful of the evaluation system we are using.

DR. PATTEN: We think the system that we use is reliable, and we have published our interobserver correlations that are extremely high so that the head holding and leg holding are reproducible.

DR. MUNSAT: Let me comment. You know correlation is not what it seems to be. For example, if you have a scale where you rate people as only 1 or 2, then you are going to get a correlation of 99.9% in terms of intra- and inter-rater reliability, so one has to be careful about correlation cautions.

DR. PATTEN: I agree with you on what you said about the Medical Research Council Scale. We don't think this is quantitative at all and doesn't reflect real numbers at all. We think there are defects in all strength data, but our numbers came out 7%/year on the average, and for what it is worth, that is the percentage of strength lost per year for the patients.

DR. WINDEBANK: Can I take issue with you about the tests that you recommend doing on all patients? It seemed like a very extensive battery of tests, particularly sural nerve biopsy. I think the concept of doing sural nerve biopsy in every patient if they don't have any clinical evidence of peripheral neuropathy is both overinvasive and not cost-effective.

DR. PATTEN: We did not biopsy every patient. We did biopsy patients who had slowed sural nerve conduction velocities, and in that case, I think the yield is high. We think that it made a major contribution to the therapy of some of the patients where we thought we were dealing with a nontreatable post-polio syndrome, and it actually turned out to be something that was inflammatory and treatable.

Glossopharyngeal Breathing and Noninvasive Aids in the Management of Post-Polio Respiratory Insufficiency

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INTRODUCTION

Acute respiratory failure was not an uncommon complication of paralytic poliomyelitis during the prevaccine epidemics earlier in this century. Tracheostomy with tracheostomy intermittent-positive pressure ventilation (TIPPV) or iron lung negative pressure aid were the two classic methods of managing this problem [1, 2]. Many of these people have remained respirator-dependent since the onset of polio. Many others, freed from respiratory assistance since their acute polio, are once again requiring respiratory aid [2, 3].

Possible acute complications of tracheostomy include hemorrhage, endobronchial intubation, pneumothorax, pulmonary oxygen toxicity, subcutaneous emphysema, wound infection, gastrointestinal complications, and positive water balance. Later complications may include impingement and erosion of the subclavian artery, tracheomalacia, pneumothorax, atelectasis, granuloma with stomal stenosis, and hemoptysis [4], increased secretions, mucous plugging, persistent Gram-negative tracheobronchial colonization [5], and recurrent purulent bronchitis [4]. Tracheostomy site leakage, even with the tube plugged, decreases the effectiveness of the patient's cough and glossopharyngeal breathing (GPB) efforts.

The iron lung has not been a convenient alternative to tracheostomy because it requires that the patient be immobile during its use. New portable iron lungs are not practical for 24-hour use for the same reason. Neither pneumobelt nor chest shell ventilators are consistently effective alternatives. Neither is adequate in the presence of severe scoliosis. The chest shell is ineffective in the erect position. The pneumobelt is not effective when its

wearer is supine. Neither is capable of delivering the occasional deep breaths ("sighs") that are important in preventing microatelectasis, maintaining normal lung compliance, and assisting pulmonary toilet by allowing a more effective cough. Although these devices can provide adequate ventilation for many patients over a period of years, hypoventilation is frequent, especially with the decreased lung compliance that develops over a period of years.

Shortcomings of negative pressure techniques for 24-hour support, as well as the dangers and discomfort of TIPPV, have led to the development and use of mouth intermittent-positive pressure ventilation (MIPPV) complemented by GPB. Although these techniques may be used in the presence of a plugged tracheostomy tube, they are most effective without a tracheostomy. They can be employed in managing patients who have been respirator-dependent since onset of polio, as well as those with late-onset respiratory insufficiency.

MOUTH INTERMITTENT POSITIVE PRESSURE VENTILATION (MIPPV)

The process of MIPPV provides assisted ventilation with a positive pressure ventilator via a mouthpiece held or fixed in place at the mouth. It is ideal for home management and may be used up to 24 hours a day. This is necessary for the majority of our patients, many of whom have vital capacities (VC) approaching 0 cc. During the daytime, a portable positive pressure ventilator may be mounted on the back of a motorized wheelchair with a modified frame.

The Goldwater frame (Fig. 1) has 4 horizontal bars for reinforcement instead of crossbars that permit the wheelchair to collapse. Although less portable because of its rigid frame, the wheelchair has space under the seat for two 12 volt batteries for chair operation and another to operate the respirator. A battery charger, and the respirator itself, are mounted on a tray behind the back of the chair (Fig. 2). The mouthpiece is brought to the front of the chair and held adjacent to the patient's mouth by a gooseneck clamp attached to the frame. This permits the patient to take assisted breaths as needed, while allowing his mouth to be free to operate the motorized chair and perform other activities (Fig. 3). Many patients with little or no time free of MIPPV prefer to have the mouthpiece free of the gooseneck clamp so that they can keep it in their mouths continuously (Fig. 4). This has the advantage of permitting greater freedom of neck movements.

For MIPPV during sleep, the Bennett lip seal (Fig. 5), which holds the mouthpiece firmly in the mouth, is usually recommended. The patient develops reflex muscle contractions of his lips, cheeks, and soft palate to prevent leakage of insufflated air. For the occasional patient with an incompetent soft palate, cotton pludgets, face mask, or other modifications may be

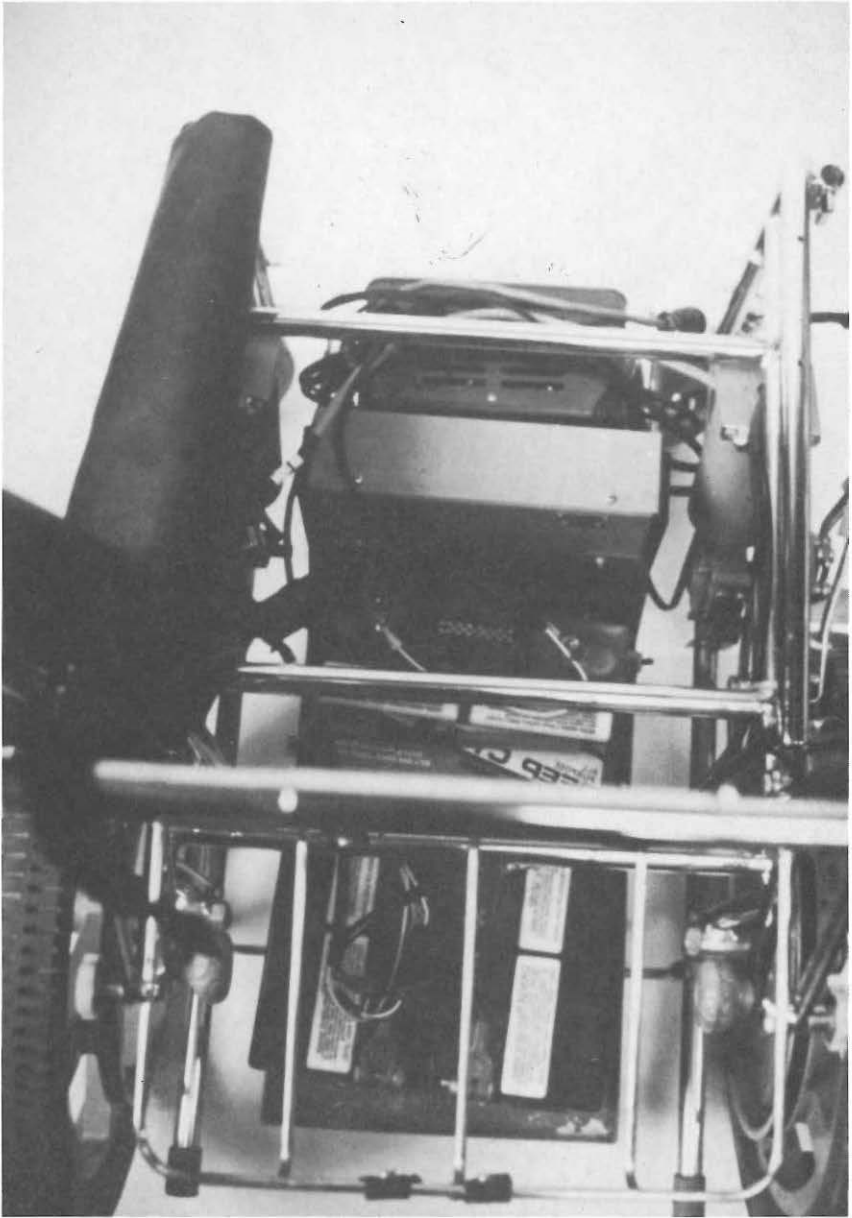


Fig. 1. Goldwater frame with 4 horizontal bars for maximum support and space for respiratory equipment.

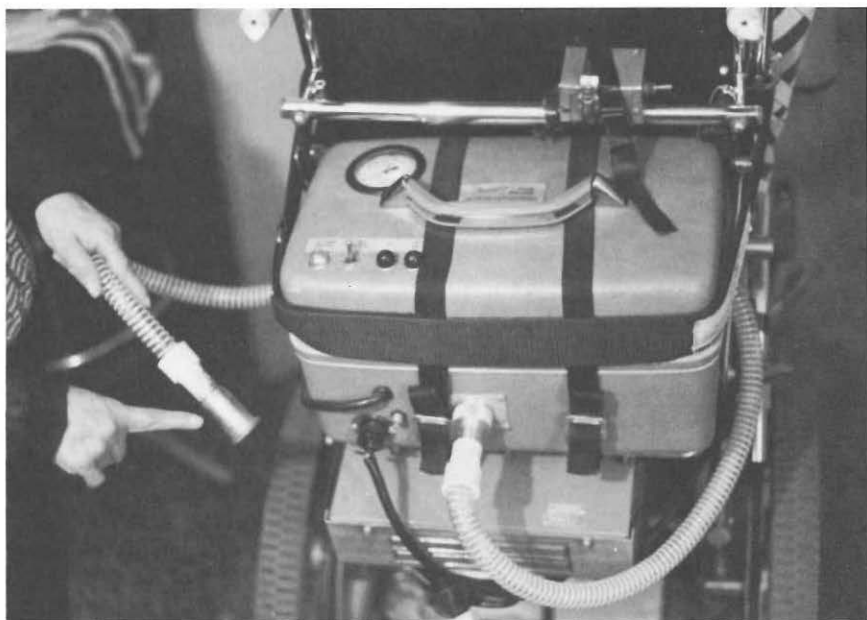


Fig. 2. Installation of portable ventilator and underlying charger.



Fig. 3. Patient with sip and puff motorized wheelchair. Mouth piece for MIPPV is supported adjacent to sip and puff control by gooseneck clamp attached to wheelchair frame.



Fig. 4. Patient using MIPPV with mouthpiece in her mouth at all times.

necessary to prevent excessive nasal leak. Many patients have short periods of excessive leak and hypoventilation during sleep from which they recover spontaneously. The success of this technique in normalizing ventilation and prolonging life has been described for patients with Duchenne muscular dystrophy [6, 7].

A study of the use of MIPPV as a predominant form of respiratory aid in the management of 75 post-polio respirator-dependent patients was undertaken [8]. In that study, patients were separated according to their mode of noninvasive respiratory assistance. Forty-three patients with an average VC of 607 cc relied on MIPPV alone for 24 hours a day. Twenty-three others with an average VC of 485 cc combined MIPPV with other noninvasive techniques for total assisted ventilation. Nine other patients described in the study used MIPPV overnight, but with an average VC of 1034 cc, were able to get by with only short periods of assistance during the daytime. Only 6 of these 75 patients eventually required tracheostomy placement for management of excessive secretions, acute cardiopulmonary episodes, or other medical complications. For the total of 75 patients, the average length of MIPPV dependence was 14 years 5 months per patient.

In our present study of 80 patients requiring respiratory assistance, 3 groupings were observed. Group 1 consisted of 44 persons respirator-



Fig. 5. Bennett lip seal with straps for above and below the ear to secure the mouthpiece for overnight MIPPV.

dependent since onset of polio. Group 2 consisted of 22 persons who became dependent on respiratory aid months to years after onset of acute polio and who currently have no significant time free of their aid except by GPB. Group 3 consisted of 14 persons who require MIPPV only overnight and are free of ventilator use for most of the daytime. The most recent VCs and techniques of noninvasive assistance employed are indicated in Tables 1–3.

TABLE 1. Patients Ventilator-Dependent Since Onset of Polio

Number of patients	44
Deceased	14
Average age of living, years	50.1 (21–71)
Average age at death, years	39.7 (18–56)
Average age at onset of polio and ventilator dependence	17.5 (2–44)
Years on iron lung, chest shell, rocking bed prior to MIPPV, 40 patients, average	15.2 (2–34)
Years on MIPPV, average	15.2 (2–30)
Average vital capacity, cc	505 (0–1700)
Number of patients on MIPPV alone	23
Number of patients with tracheostomy	3
Years of MIPPV prior to tracheostomy, average	16.7
Years of TIPPV, average	2.3

TABLE 2. Patients With Late-Onset Respiratory Failure Requiring Full-Time Aid

Number of patients	22
Deceased	4
Average age of living, years	44.5 (27-63)
Average age at death, years	48.0 (26-62)
Average age at onset of polio, years	12.7 (0-30)
Average age at onset of ventilator dependence	30.2 (5-53)
Years on iron lung, rocking bed, chest shell prior to MIPPV, 5 patients, average	8.6 (2-21)
Years on MIPPV, average	12.5 (3-27)
Average vital capacity, cc	740 (180-1600)
Number of patients on MIPPV alone	20
Number of patients with tracheostomy	3
Years of MIPPV prior to tracheostomy, average	6.3 (3-10)
Years of TIPPV, average	2.0 (1-4)

Table 1 demonstrates the tendency to switch from the rocking bed and the negative pressure assistance of the iron lung and chest shell to MIPPV after years on these techniques. This is due to the increased efficacy and convenience of MIPPV for most patients. In this group, MIPPV use has been effective for an average of 15.2 years despite an average VC of only 505 cc. More than half of the patients use MIPPV alone 24 hours a day. The other 21 patients combine it with pneumobelt use during the day, or the rocking bed or chest shell overnight for full-time respiratory aid.

Table 2 demonstrates that the majority of our patients (17/22) with late-onset respiratory insufficiency have gone directly to MIPPV use. Five patients employed other techniques for an average of 8.6 years prior to switching to MIPPV. Twenty of 22 patients currently use only MIPPV around the clock.

All of the patients in Table 3 with recent onset of respiratory insufficiency presented predominantly with symptoms of sleep hypoventilation. They have resorted to MIPPV alone for their only mechanical aid. This group's VC is significantly greater than that of patients in groups 1 and 2, but as the VC decreases significantly each year [2], dependence on MIPPV and GPB up to 24 hours a day may be anticipated in the future.

TABLE 3. Patients Dependent on Overnight MIPPV Use Only

Number of patients	14
Average age at onset of polio, years	10.5 (0-25)
Average age at onset of overnight MIPPV, years	39.5 (20-57)
Average current age, years	44.8 (31-59)
Most recent vital capacity, average cc	1060 (690-1720)
Years on MIPPV, average	5.9 (0.5-14)

GLOSSOPHARYNGEAL BREATHING (GPB)

GPB is a technique whereby a person uses pistoning action of the tongue to project a bolus of air into the trachea. Immediate vocal cord closure traps the bolus in the bronchial system. Each pistoning action of the tongue (gulp) provides an added bolus of air and, therefore, a deeper breath. Soft palate closure of the nasopharynx prevents leakage of the bolus out of the nose. With practice, people can take up to 200 cc boluses with each gulp. One breath might consist of 6 to 65 gulps. The glossopharyngeal maximum single breath capacity (GPmaxSBC) is defined as the GPB-assisted inspiration a patient can manage with unlimited gulps. The patient begins GPB "on top" of a maximal voluntary breath. The GPmaxSBC is, therefore, equal to the VC assisted by GPB. GPmaxSBC of over 3 liters is not uncommon by patients with VC under 500 cc and adequate glossopharyngeal muscles. With practice, patients increase gulp volumes and improve GPB efficiency. Effective use of GPB by a patient with paralytic respiratory insufficiency will permit a more effective cough, decrease atelectasis, improve lung compliance, allow more normal speech, and reduce dependency on mechanical assistance. This technique can be an effective backup in the event of respirator failure. It sustains people while switching modes of mechanical assistance. Some require GPB for smooth operation of a motorized wheelchair, since one can not await a respirator cycled breath when immediate air is necessary for control. Figure 6 shows the tracing of a patient who requires GPB for sip and puff wheelchair operation.

The use of GPB is compatible with all currently available forms of portable noninvasive respiratory assistance. It is particularly beneficial when used concurrently with forms of aid such as the pneumobelt or MIPPV during normal daytime activities.

We have reviewed the use of GPB by 49 patients trained in its use. Yearly reevaluations were performed to monitor the patient's GPmaxSBC, minute ventilation by GPB at the patient's natural, most comfortable rate and depth (regular GPB minute ventilation), and the maximum minute ventilation by maximal depth GPB assisted breaths (maximum GPB minute ventilation). Frequency of GPB-assisted inspirations per minute, gulps per glossopharyngeal breath, and ccs of air per gulp were also noted.

Three patterns of GPB use were observed (Table 4). Although data for GPB in the sitting position are indicated, volumes are generally equal to or greater than this in the supine position or with use of an abdominal binder.

The 26 patients in group 1 use GPB throughout the day for a smooth natural speech pattern, volume, and duration despite dependence on a cycling ventilator. These patients may use GPB for safe operation of a motorized wheelchair. In some cases they use it for time free of MIPPV or other aid for many hours a day. They may also use it for reasons noted below.

The 10 patients in group 2 use GPB when changing between MIPPV and

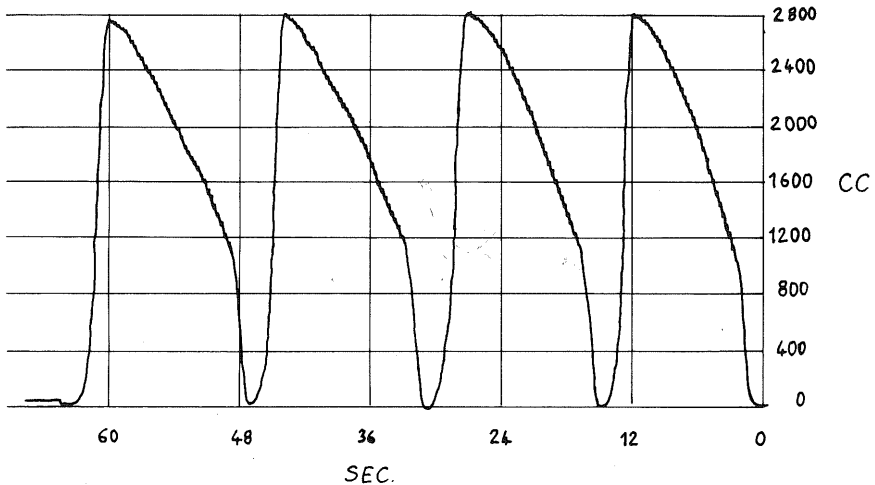


Fig. 6. Maximum minute ventilation by maximal glossopharyngeal breath assisted inspirations. Maximal minute GPB minute ventilation 11.2 lt/min by a patient with a vital capacity of 1.09 lt, GPmaxSBC 2.8 lt, average 30 gulps per GPB assisted breath, 77 cc/gulp.

some other form of respiratory aid. They use it during transfers, for assisted coughing, “sighing,” and as a backup in the event of respirator failure.

The 13 patients in group 3 failed to practice the technique and were not evaluated in its use.

Table 4 demonstrates that patients can inflate their lungs to an average of 2 to 6 times their VC by GPB alone. Some patients with VCs of 0 cc have GPmaxSBC recorded to about 3 liters (lt) and can be free of ventilator aid for long periods of time by GPB alone.

Case Study 1

This 46-year-old man contracted polio in August, 1955 at age 15 years. His maximum GPB minute ventilation and regular GPB minute ventilation spirometric tracings are shown in Figure 7. His VC has been 0 cc since onset of polio and he remained in an iron lung for one year. He was then maintained on the chest shell ventilator overnight and the pneumobelt during the day from 1956 to 1981. In 1981, when the chest shell was no longer providing optimal ventilation, he switched to overnight MIPPV with the Bennett lip seal. He has never had a tracheostomy.

He was introduced to GPB in 1956 and has had GPmaxSBC of 1.09 to 2.22 lt on yearly evaluations. His most recent GPmaxSBC in August 1986 was 1.8 lt. His maximal GPB minute ventilation was 8.49 lt with 5 glossopharyngeal breaths of an average of 20 gulps each, 1.67 lt/breath (84 cc/gulp) over

TABLE 4. Most Recent GPB Evaluation of 49 Post-Polio Patients, Sitting Position

	No. of Patients	VC cc average	VC % of Pred	Most Recent GPmaxSBC (1t)	Gulps	cc/Gulp	Highest GPmaxSBC (1t)
Group 1	26	330 (0–740)	9.6 (0–19)	1.81 (0.91–2.93)	19.9 (8–41)	83 (40–140)	2.21 (1.03–3.41)
Group 2	10	734 (430–1170)	16.6 (13–34)	1.59 (1.09–3.40)	13.2 (6–27)	92.1 (49–158)	1.81 (1.11–3.40)
Group 3	13	598 (320–855)	17.8 (10–24)	do not practice glossopharyngeal breathing			

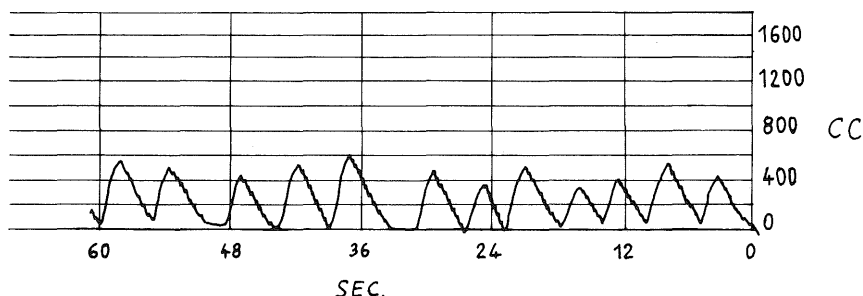
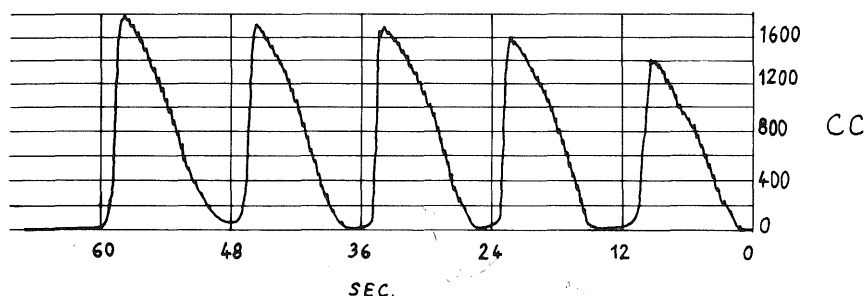


Fig. 7. Top: Maximal GPB minute ventilation 8.39 lt, GPB inspirations average 1.67 lt, 20 gulps, 84 cc/gulp for each breath in a patient with a vital capacity of 0 cc.

Bottom: Same patient regular GPB minute ventilation 4.76 lt/min, 12.5 breaths, average 8 gulps per breath, 47.5 cc/gulp performed over one minute period.

the course of 1 minute (see Fig. 7 top). This compares favorably to the 7.83 lt/min ventilation (rate 22, average delivered volume 350 cc), which he receives from daytime pneumobelt use. His regular GPB minute ventilation is 4.76 lt/min (12 glossopharyngeal breaths of 8 gulps each, 380 cc average volume per breath) (see Fig. 7 bottom). He breathes comfortably in this manner for hours of time free from mechanical aid while maintaining normal O_2 saturation, pCO_2 , pulse, and blood pressure. This provides him with backup in the event of respirator failure and permits him to transfer between the pneumobelt and MIPPV. It allows him essentially natural speech production, which is the main reason that he employs the technique throughout the day. He also uses it for coughing, "sighing," and shouting when necessary.

On several occasions, his chest shell ventilator ceased to function as he slept. He awoke GPB before gaining any awareness of what had happened.

Case Study 2

This was one of those rare people who went throughout the day without mechanical respiratory aid by employing GPB despite a VC of 0 cc since the onset of polio. He contracted polio at age 7 years in 1951. He was maintained in an iron lung until 1958. He learned GPB in 1961 which, when combined with MIPPV, freed him from the iron lung during the daytime. His GPB skills peaked in 1967 (Fig. 8) and plateaued until 1982, one year prior to his death. By 1972–1973 his regular GPB minute ventilation exceeded 6 lt/min, with a relaxed glossopharyngeal breath tidal volume average of 1.23 lt, 5 breaths/minute (15 gulps, 94 cc/gulp). This allowed him to be off mechanical aid throughout the daytime when awake. At one evaluation, his $p\text{CO}_2$ was 31 mm Hg following 8 continuous hours of GPB. Until 1980, he was able to leave his respirator when leaving home, by relying on GPB alone. He supplemented GPB with MIPPV when convenient during the daytime, especially during meals. His pulmonary function was not significantly changed until 1980, when low normal diffusion capacity was noted. In 1982, $p\text{CO}_2$ on GPB exceeded 40 mm Hg for the first time (44 mm Hg), GPmaxSBC decreased, and signs of right ventricular hypertrophy developed. He died in 1983 as the result of complications of lower limb cellulitis.

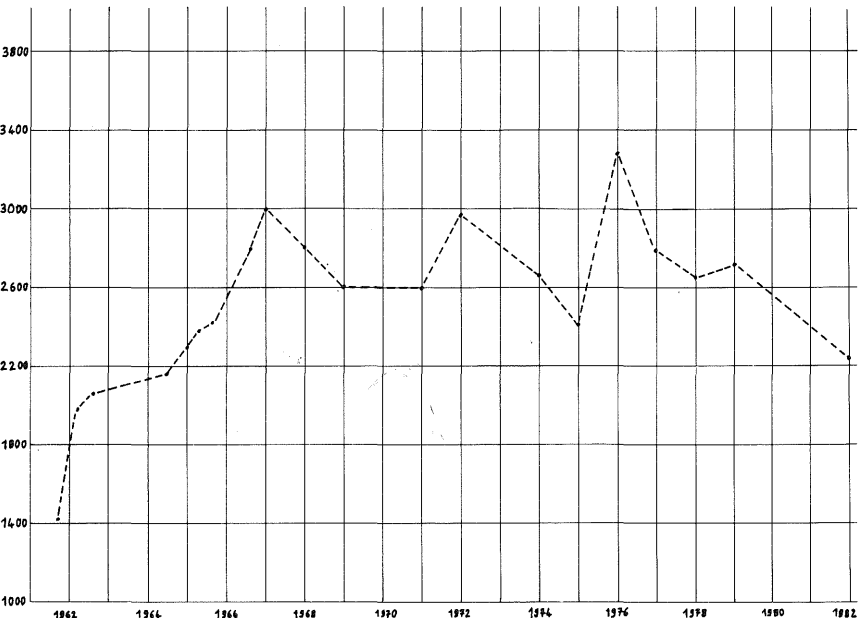


Fig. 8. Yearly evaluations of GPmaxSBC for a patient with a vital capacity of 0 cc.

In 1973, this man mastered the use of the Bennett lip seal for MIPPV overnight. He no longer required the iron lung, which he had used for 22 years. Trials of chest shell and rocking bed mechanical aids were undertaken but tidal volumes delivered never exceeded 400 cc and were inadequate for this patient. He used MIPPV with the Bennett lipseal as his only mode of overnight respiratory assistance until his death in 1983.

CONCLUSION

This study has demonstrated the effectiveness of MIPPV complemented by GPB as an alternative to TIPPV and other less versatile modes of assistance in the management of severe respiratory insufficiency in patients with post-polio syndrome. As noted, this combination has been shown to be effective for patients with other conditions as well [6, 7], including those with intrinsic lung disease [9]. Although it seems to be of greatest benefit to patients with paralytic respiratory failure and normal lung parenchyma, its use should be explored for any patients experiencing acute or chronic respiratory insufficiency who are alert and have adequate oropharyngeal musculature.

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DISCUSSION

DR. WIECHERS: In your experience, are you finding that the older polio patients, who for the first time, are having to use some type of assistive device at night, prefer intermittent positive pressure with a lip seal device over other respiratory aids?

DR. BACH: In general, yes, because it does simplify the type of equipment that they have to use and it gives them the ability to take as deep a breath as they want. You do not have to have both negative pressure and positive pressure equipment or a larger nonportable ventilator that does both. You can also use your positive pressure ventilator to operate a pneumobelt. MIPPV also permits more bed mobility than the use of negative pressure body ventilators. It is easier and quicker to set up, and most patients find the use of the Bennett lipseal to be comfortable and reliable.

DR. FUGL-MEYER: What is your percentage of failure in teaching people glossopharyngeal breathing (GPB)?

DR. BACH: Less than one-third of the patients, although trained for several weeks, did not master the technique, or if they did master it, they just never used it. There is some indication from some preliminary information that patients with complicating obstructive lung disease do not gain significant periods of freedom from mechanical respiratory aid by glossopharyngeal breathing. So the technique is not going to provide complete freedom from ventilators in every patient, but for patients who use it all day, it allows them to speak normally and to even shout, which they would not be able to do otherwise.

DR. FISCHER: I have also seen patients prefer to die than to have a tracheostomy, which I think is very foolish. The polio patients, as they get older, begin to lose their functional ability and they often cannot GPB as well and the lungs get stiff, so the trach can be a new lease on life. I think you obviously want to go without it until you have to, but it should not be put off too long.

DR. BACH: Well, we have been able to put it off in some patients for 30 years, and these are patients dependent on respiratory aid 24 hours a day, including patients with 0 cc vital capacities. They use MIPPV during their sleep; in fact, one patients (*Case 1*) was on a chest piece from 1956 to 1981 before switching to MIPPV when his lungs stiffened to the point that the chest shell no longer maintained normal blood gases. He awoke on several occasions from sudden failure of his chest piece and he awoke glossopharyngeal breathing without

even realizing what he was doing. So the use of GPB and MIPPV can be effective for these patients even in the presence of decreased pulmonary compliance and VCs of 0 cc. I think that we have to consider tracheostomy when we have severe intrinsic lung disease, complicating medical factors, or poor patient compliance for the noninvasive techniques.

Sleep-Disordered Breathing as a Late Effect of Poliomyelitis

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The survivors of the poliomyelitis epidemics of the 1940s and '50s have confronted the functional losses resulting from the initial attack of the virus and, for the most part, have accepted their disability with remarkable equanimity. However, late progression of functional loss in muscles previously affected by polio has been observed [1-5]. Recently, we have observed increasing numbers of polio survivors with sleep-disordered breathing associated with daytime somnolence. This symptom-complex has been recognized in recent years and was reported at the First Research Symposium on the Late Effects of Poliomyelitis in 1984 [5] as one of the observed respiratory complications. This paper presents further observations of the sleep apnea syndrome in polio survivors.

METHODS

Questionnaires regarding sleep problems were mailed to all members of the Polio Survivors Association of Downey, California. There were 165 respondents. An additional 27 patients were seen in the office this year with symptoms suggesting sleep apnea. The results of the analysis of this experience will be discussed. The subjects included in this study all experienced daytime sleepiness. Those who gave histories suggesting sleep problems without daytime somnolence were excluded.

RESULTS

Table 1 presents the results of an early response to the questionnaire. The control group was obtained from employees undergoing annual physical examinations at the employee health clinic. This table clearly demonstrates the extent of the sleep problem in the polio survivors. Table 2 presents the frequency of daytime sleepiness by gender, and Table 3 presents the sleep problems described by 75 respondents who exhibited daytime somnolence.

TABLE 1. 1986 Polio Survivors Questionnaire: Respondents Reporting Sleep Problems

	155 Polios	90 Controls
Wake frequently?	92 (59%)	7 (8%)
Snore?	61 (39%)	7 (8%)
Sleepy during day?	63 (41%)	5 (6%)
Average age	56	50

Twenty-seven persons were evaluated as outpatients, 17 women and 10 men. The average age was 51. Nine individuals, or one third of the group, gave histories suggesting sleep-disordered breathing. One individual required assisted nighttime ventilation with a cage and wrap. One who now uses a PLV 100 by tracheostomy for nighttime ventilation was observed to have central apneic episodes. A third patient, who gave a history suggesting nocturnal apnea, was experiencing somnolence and fatigue during the day. He was advised to have a sleep study in San Francisco where he lives. One patient with residual pharyngeal weakness had episodes of waking with choking spells. Five patients were prescribed protriptyline [6]. One of them who had tried a cuirass without satisfaction did respond to protriptyline. One described nighttime apneic episodes at his home, which had an elevation of 6,000 feet. He was prescribed protriptyline, and it was recommended that he use oxygen while sleeping. Two other patients with sleep-disordered breathing received protriptyline; one of these also required nighttime oxygen. Recently, a patient with residuals of bulbar polio was seen in the office with symptoms of sleep deprivation. Her family described apneic episodes during sleep suggesting central origin. She had required a tracheostomy in recent years, which she retained, but was not using assisted ventilation. Her arterial carbon dioxide tension was 58 mm. She was scheduled to be admitted for ventilator trials.

DISCUSSION

The recognition of unusual patterns of breathing during sleep has a long history in nonmedical literature. Shakespeare's Falstaff and Dickens' Joe, of the "Pickwick Papers," are classic examples: "Falstaff!—fast asleep behind the arras, and snorting like a horse . . . Hark, how hard he fetches breath . . ." [7]. The study of sleep in this country began with Nathaniel Kleitman's [8] first published scientific work on sleep disorders in 1939, which was updated in 1963. In 1978, Guilleminault and Motta [9] described sleep apnea as a late

TABLE 2. 165 Respondents to 1986 Polio Questionnaire

	Average Age	Daytime Sleepiness
Male 31% (51)	55	20 (39%)
Female 69% (114)	53	55 (48%)

TABLE 3. Sleep Problems Reported by 75 Respondents (45% of Total) Who Experienced Daytime Somnolence (1986)

	Sleep Poorly	Wake Frequently	Snore	None
Women	52 (95%)	45 (82%)	26 (47%)	9 (16%)
Men	17 (85%)	16 (80%)	15 (75%)	3 (15%)
Total	69 (92%)	61 (81%)	41 (55%)	12 (16%)

effect of poliomyelitis. They studied 5 patients between 1970 and 1976. Each complained of daytime sleepiness and all had contracted poliomyelitis at least 16 years before consulting the authors. All 5 gave a history of bulbar involvement and 2 had required ventilators during the early months of recovery. The symptoms began about 2 years before referral. The apneic episodes included central only (52%), obstructive only (16%), and mixed (32%). The longest episodes occurred during rapid eye movement (REM) sleep and were associated with the lowest oxyhemoglobin saturations. All 5 patients were placed on cuirass respirators. The authors discovered that frequencies above 12 to 13 resulted in an increase of obstructive episodes. This was corrected by lowering the frequency to 8 to 10 cycles per minute. The tank respirator also aggravated obstructive apnea if the rate was not adjusted properly. The options for the sleep apnea problem in polio survivors, in addition to negative pressure respirators, include mouth-positive pressure devices, such as the Bennett mouth-seal, which can be used with cycled ventilators, and, of course, tracheostomy with volume-cycled positive pressure. When the technology of phrenic nerve pacings first appeared in the news several years ago, the polio survivors naturally called to ask if they could benefit from this procedure. Of course, the nerve pacer cannot work without a viable phrenic nerve, which is what these people lack. Pneumobelts can still be useful for respiratory assistance when the individual is in the upright position, but few, if any patients use it as a ventilator for sleep. Rocking beds, still in use in our area, may benefit some patients with central sleep apnea. I have no experience with this modality for people with sleep-apnea syndrome, but it may be worth exploring before resorting to more invasive measures. Nasal continuous positive pressure (nasal CPAP) can be effective in obstructive apneas [10] but is unlikely to benefit patients whose sleep apnea is primarily central.

Why is poliomyelitis infection associated with late-onset sleep apnea syndromes? Why does obstructive apnea occur as frequently as it does, often with a central element? Cherniack [11] postulated instability in the feedback control system while Suratt [12] proposed a dissociation of the coupling of the upper airway and thoracic muscle activity, which occurs predominantly during REM sleep. High bulbar lesions have often resulted in central apnea in these people. Most people with frequent apneas of central origin will require

respirators, as will many with mixed apneas. The latter group will often require tracheostomy. Guilleminault [13] has discussed the pathogenesis of the sleep apnea syndromes in detail. This and other publications from the Stanford Sleep Disorders Center are recommended.

Is a similar mechanism responsible for the sleep-disordered breathing of the obese hypoventilator and the neuromuscular groups? Probably the excess respiratory load is common to some individuals with musculoskeletal deformities secondary to polio, but the involvement of respiratory neurons in poliomyelitis seems to be a common denominator in our patients. However, there are probably multifactorial components in sleep apnea. It has been noted [13] that once adequate ventilation and oxygenation during sleep are established in patients (including polio survivors), the obstruction may disappear, confirming a complex interaction between central and obstructive components.

Sleep apnea is a relatively recently recognized late effect of poliomyelitis. This paper presents a surprisingly high frequency of this problem: 45% of a group of 165 polio survivors reported daytime sleepiness and 92% of these reported that they slept poorly, usually waking frequently and often reporting snoring. We hope to study a random population of polio survivors in our community with polysomnography to establish the true nature and frequency of this problem.

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DISCUSSION

DR. BUCHHOLZ: I have a number of comments. The first comment is that it is well known that people are notoriously poor judges of their degree of sleepiness or the wellness of their nocturnal sleep. That is why it is so important to objectively evaluate these issues. Sleep apnea is often variable between REM and nonREM sleep, therefore one must look at the full cycle of sleep. Cardiac arrhythmias have to be looked for with EKG monitoring. The degree of oxygen desaturation is important in deciding how aggressively to treat the condition. What I am saying is that I think that someone with suspected sleep apnea really deserves a complete sleep study, including nighttime and daytime studies.

The second comment is that most people treating sleep apnea have not had the kind of success that you mentioned with Vivactil. Vivactil probably works in most cases by suppressing REM sleep, during which most sleep apnea occurs or is worse. It is poorly tolerated in many men because of its anticholinergic properties causing impotence.

You didn't mention, and perhaps you have tried these other measures in some patients: things like continuous positive airway pressure (C-PAP), which is rapidly gaining popularity among people treating sleep apnea. A relatively benign and very effective method for overcoming sleep apnea is by applying a facial mask, or in terms of surgical options, the use of uvulopalatopharyngoplasty (UPPP), which is certainly a much more cosmetically acceptable procedure than a tracheostomy.

DR. FISCHER: Speaking from last first, the UPPP has been found to be quite effective in reducing snoring, but the latest word from the sleep labs in our part of the country is that it's not effective in sleep apnea.

DR. BUCHHOLZ: The data that I am aware of from places across the country suggest that UPPP has generally been effective in at least half and, in some centers, in as many as three-quarters of the patients with obstructive sleep apnea. There clearly is a problem in selecting which patients it would benefit, but I would certainly advocate it as a surgical option before the tracheostomy.

DR. FISCHER: We do use C-PAP when it is tolerated for continuous positive airway pressure and, when it works, it works well. I think it is worth a try before you do a tracheostomy.

DR. ALBA: I just wanted to comment on Dr. Buchholz's comments. On the use of C-PAP, you have to have active abdominal muscles because you do change the muscles that you are using in quiet breathing to include some forced expiration to overcome the positive pressure on your airway. If you are a polio patient, you have to have the abdominal muscles to be able to do that. In UPPP you have to worry about the fact that you may lose your frog breathing capability because you may lose air volume through the nose because of resection of the soft palate.

DR. MONRO: We have studied something like 200 patients with polysomnography who have had a post-viral syndrome, some of whom have had post-polio in which a very high incidence of sleep apnea occurs, both obstructive and central. With the obstructive type, we have found that postural positioning of the patient often can help, and we have used a number of very simple remedies for the patients. One of them is Slophylline, a theophylline derivative, in a very small dose as a stimulant. It has been very effective in many of the patients. The delivery of oxygen at $1\frac{1}{2}$ liters per minute generally by nasal flow is a very simple remedy, and it works extremely well.

Pain In Post-Poliomyelitis—Addressing Causes Versus Treating Effects

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Pain interfering with work, activity, and the quality of life and which has persisted for months or years is a major problem for persons experiencing the late effects of poliomyelitis [1, 2]. In a series of 114 confirmed post-polio patients seen in an outpatient clinic, 102 or 90% reported pain as a chief complaint (Table 1). All of those who used their upper limbs for locomotion reported pain as limiting their ability to function. The location of pain is related to use (Table 2). Ambulatory patients reported a high incidence of back and hip pain and diffuse lower limb muscle pain. Those using crutches and wheelchairs reported neck and back pain and injuries to the upper limbs. Most people described having used several treatment measures such as medications, rest, heat, or exercise with only temporary relief of pain. Our pain management program is directed toward the causes of pain and is focused on restoring skeletal alignment, reducing energy expenditure for the task, and providing assistance to muscles that are working at abnormally high levels of their capacity.

The pain stems from the fact that the body has an extraordinary ability to maintain function in the presence of muscle weakness and skeletal abnormalities (Fig. 1). The body does so, however, at the biologic price of increasing energy expenditure for the task, placing excessive and abnormal forces on joint structures, and requiring increasing work from innervated muscles. Such daily compensations occurring over years lead to overstretched ligaments, degenerative joint changes, and decompensation of weakened muscles [2, 3].

POSTURAL ABNORMALITIES

The post-polio patients in this series were functioning with a large number of major postural abnormalities in sitting, standing, and walking (Table 3). Most had long ago discarded assistive devices and used body compensations to achieve function. Sixty-four or over 50% of these subjects

TABLE 1. Incidence of Pain Interfering With Function in 114 Confirmed Post-Polio Patients

Method of Locomotion	No.	No. with Pain	Percent with Pain
Ambulatory no brace (independent)	67	56	84
Ambulatory with brace (independent)	12	11	92
Ambulatory with crutches (independent)	21	21	100
Wheelchair locomotion (independent)	7	7	100
Wheelchair locomotion (need personal assistance)	7	7	100
Total	114	102	90

Age: $X = 48.3$ years ($S = 11.83$) range 26–86.

Age from onset: $X = 39.1$ years ($S = 10.5$) range 25.5–85.5.

sat with an absent or reversed lumbar curve, 50 had a marked forward head and round shoulder posture, 29 were sitting with asymmetric pelvic levels, and 38 had an obvious scoliosis. The most common abnormal sitting posture was that of slumped sitting (Fig. 2B), with the weight of the trunk hanging from the posterior vertebral ligaments and the lumbar spine in a fully stretched position. This eventually leads to microtrauma and pain [3, 4].

Standing is described by many post-polio patients as causing severe pain as they wait in line or stand at work or at receptions and cocktail parties. The post-polio patient with lower limb involvement is limited to a stereotyped standing posture often accompanied by abnormalities of alignment (Fig. 3). In this series, asymmetry of the pelvic base increased in from 29 to 40 persons primarily due to uncorrected leg length discrepancies (Table 3). Twenty-nine or 38% stood on their stronger leg—a feat requiring continuous high level contractions of innervated muscles. Subjects with normal muscles, on the other hand, possess a wide variety of standing postures that use very low levels of muscle activity [5].

TABLE 2. Location of Long-Term Pain Interfering With Function in 114 Post-Polio Patients According to Method of Locomotion

	No.	Percent
Independent ambulators with or without lower limb orthoses	79	69
Back	37	47
Hip	19	24
Diffuse lower limb	18	22
Other (neck, shoulder, knee or ankle)	31	39
Locomotion performed using crutches or wheelchairs	35	31
Neck and shoulder	18	51
Back	13	37
Gleno-humeral joint	11	31
Elbow	6	17
Wrist and hand	9	26
Other (lower limb and head)	15	43

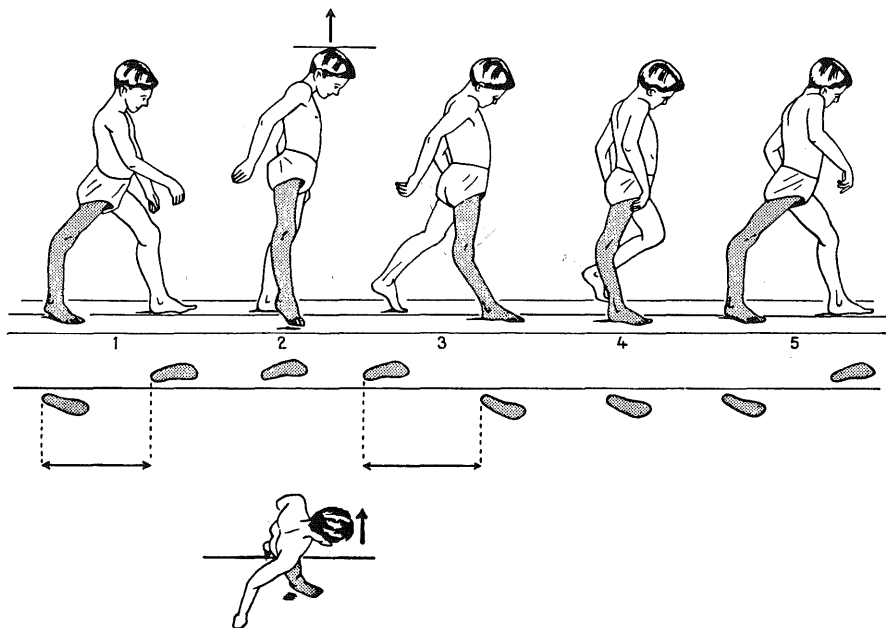


Fig. 1. Compensations of a boy with paralysis of the right lower limb due to poliomyelitis. Functional walking is performed with reliance on ligaments for stability and increased work by stronger muscles. There is marked increased energy expenditure as evidenced by the increased vertical and lateral oscillations of the body, increased arm swing, and abnormal head and trunk postures. The ligaments of the hip and knee are progressively lengthening and no longer provide stability for walking. Pain, joint dysfunction, decreased safety, fatigue, and decrease in function are imminent. (Figs. 1, 5, and 6 from Ducroquet R et al: "Walking and Limping-A Study of Normal and Pathological Walking." Philadelphia: JB Lippincott Co, 1968, with permission of the copyright holder.)

TABLE 3. Major Postural Abnormalities Occurring in Sitting, Standing and Walking in Post-Polio Patients

		No.	Percent
Posture (N)	Abnormal deviation		
Sitting (N = 111)	Absent lumbar curve	64	54
	Forward head (loss of cervical curve)	50	45
	Uneven pelvic base	29	26
	Structural scoliosis	38	34
Standing (N = 76)	Absent lumbar curve	52	68
	Uneven pelvic base	40	53
	Weight bearing on stronger leg	29	38
Walking (N = 76)	Abnormal gait deviations	76	100
	Major lateral trunk oscillations	33	43
	Obvious forward lean	40	53

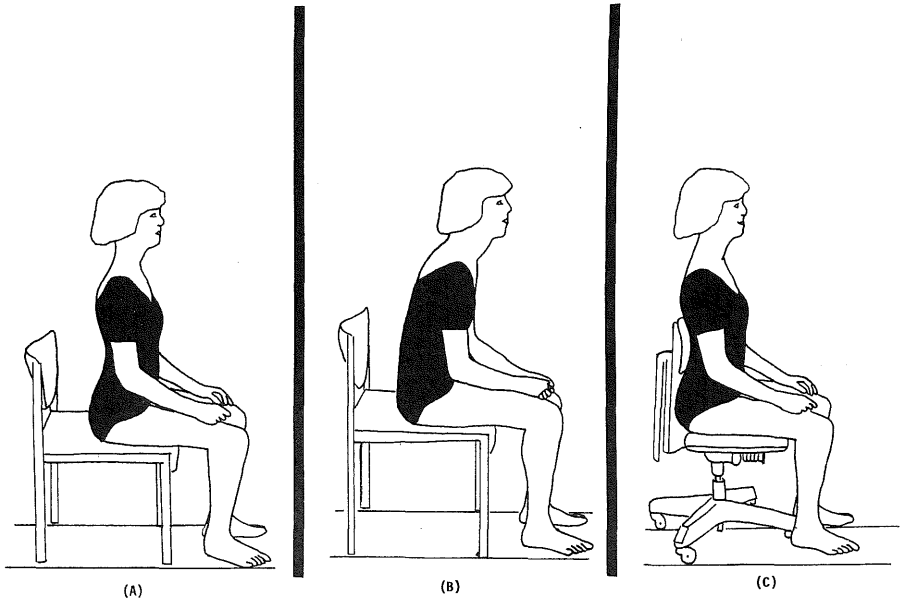


Fig. 2. A) Voluntary control of balanced vertebral weight bearing in the sitting position is short-lived. The posture can be maintained with concentration, but rapidly deteriorates when attention turns to other activities. B) Typical habitual slumped sitting posture with loss of the normal weight-bearing curves and reliance on ligamentous support. C) Mechanical restoration of vertebral curves relieves pain and permits function by reduction of continuous voluntary muscle contraction and avoidance of abnormal joint forces.

Malalignment in standing is carried into walking with the added abnormal gait deviations (Table 3). In this series, 43% demonstrated major lateral oscillations in gait. Over 50% walked with a slight forward lean at the hips and trunk (Fig. 4). The abnormal lateral oscillations of the trunk produce excessive forces on the back or knee as shown in Figure 5A, with the subject's progressive genu valgum. The forward lean is needed to prevent the knee from buckling in the presence of quadriceps muscle weakness, or to watch the floor and feet to avoid tripping and falling in the presence of ankle weakness (Fig. 1). The beginnings of this posture can be seen in the young boy with dorsi flexor muscle weakness (Fig. 6) and incorporated into the walking posture of the post-polio adult with dorsi flexion or quadriceps muscle weakness. Although the forward lean is slight, maintenance of the position requires continuous contraction of the lumbar erector spinae, which can be easily palpated manually or recorded electromyographically (Fig. 7). Such continuous and abnormal isometric muscle contractions, whether they occur in sitting, standing or walking, compress capillary beds and limit exchange

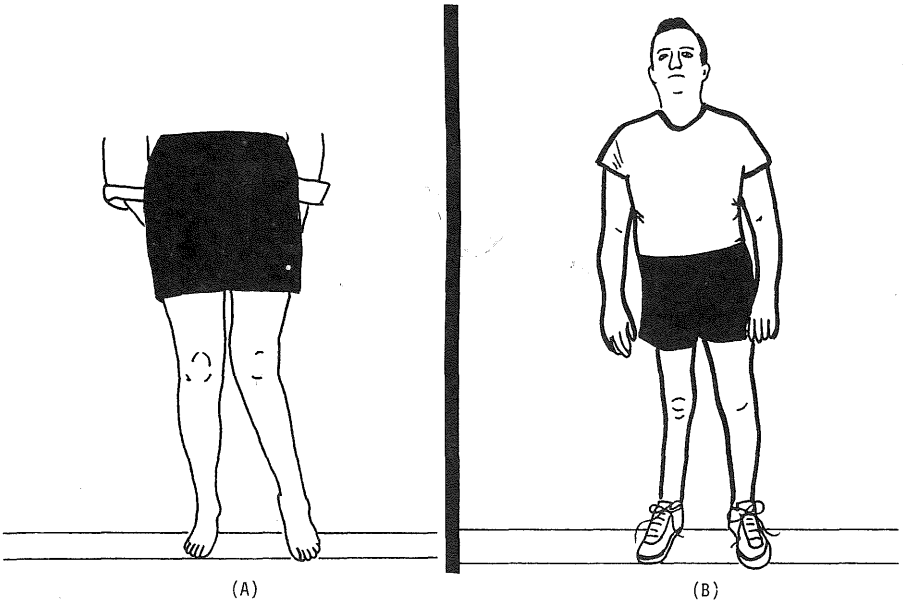


Fig. 3. Examples of the limited and stereotyped standing posture of 2 post-polio patients who have pain in both legs and back. Subject A bears weight on the stronger leg, as most commonly seen. Subject B relies on ligamentous support of the weaker leg.

between capillaries and working muscle fibers. In time, pain and dysfunction occur.

EVALUATION

Our pain management program begins with an extensive medical evaluation to identify sources of pain such as radiculopathies, spinal stenosis, nerve entrapments, peripheral neuropathies, rheumatic diseases, tumors, and other conditions.* A detailed history of new problems and current physical activities at home, at work, and in avocations is recorded, as well as physical evaluation of habitual postures in sitting, sleeping, standing, walking, and working. Although pain can be masked temporarily with medication and physical measures, long-term relief requires institution of preventive and corrective measures using mechanical or orthotic assistance and life-style modifications. This is not a readily acceptable treatment program to most post-polio patients since they equate success to discarding assistive devices and doing all the activity that other people do and more!

*In this series, 5 persons were identified with these sources of pain.

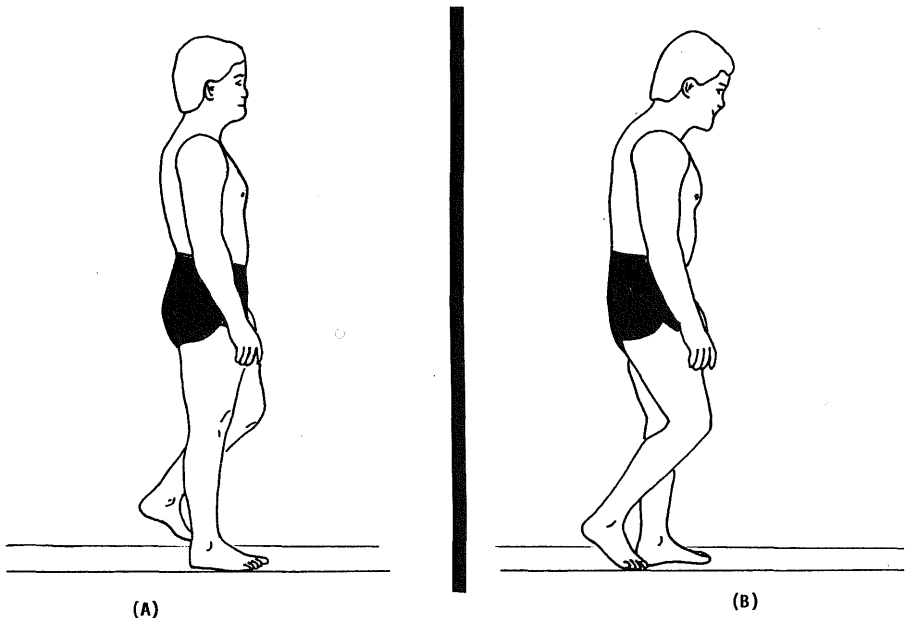


Fig. 4. A) The normal person walks erect with a lumbar curve and looking into the distance. B) Those who are concerned about tripping and falling due to muscle weakness or joint instabilities will carefully watch the floor surfaces and foot placement. Leaning forward from the hips, they have a decreased lumbar and cervical curve. In order to maintain this position, they have continuous abnormal contraction of the neck and trunk extensors.

RESTORATION OF POSTURE AND MOTION

We initiate pain intervention with the least threatening and usually most acceptable modifications in sitting and sleeping postures that occur 14 to 20 hours/day. Pain relief in sitting is most successful, as it can be demonstrated during the initial examination using lumbar rolls, wheelchair back supports, a gluteal pad, properly fitted secretarial chair, or a balans chair (Fig. 8). Our goal is to mechanically restore the lumbar curve along with the head and neck posture in order to reduce abnormal tension on ligaments or continuous muscle contractions (Fig. 2C). We evaluate seating as it occurs over hours per day at meals, at desks, in autos, in wheelchairs, and during social activities, and make recommendations for corrections. Elasticized abdominal supports and custom-made corsets are recommended for those with abdominal and back muscle weakness and trunk instability.

Sleeping surfaces and postures are evaluated for those who report neck and shoulder pain, or who report that recumbency does not relieve pain, or pain is worse in the morning. Cervical pillows are recommended for those who

primarily sleep on the side or back. Those who sleep on the abdomen are taught to avoid the extremes of head and neck rotation and external rotation of the shoulders that produce injury and pain. Most people suffering from pain during sleeping have sought firmer and harder mattresses. Instead, we recommend use of foam egg crate mattress covers or limited motion water beds, which distribute body pressures and frequently bring immediate relief of this pain.

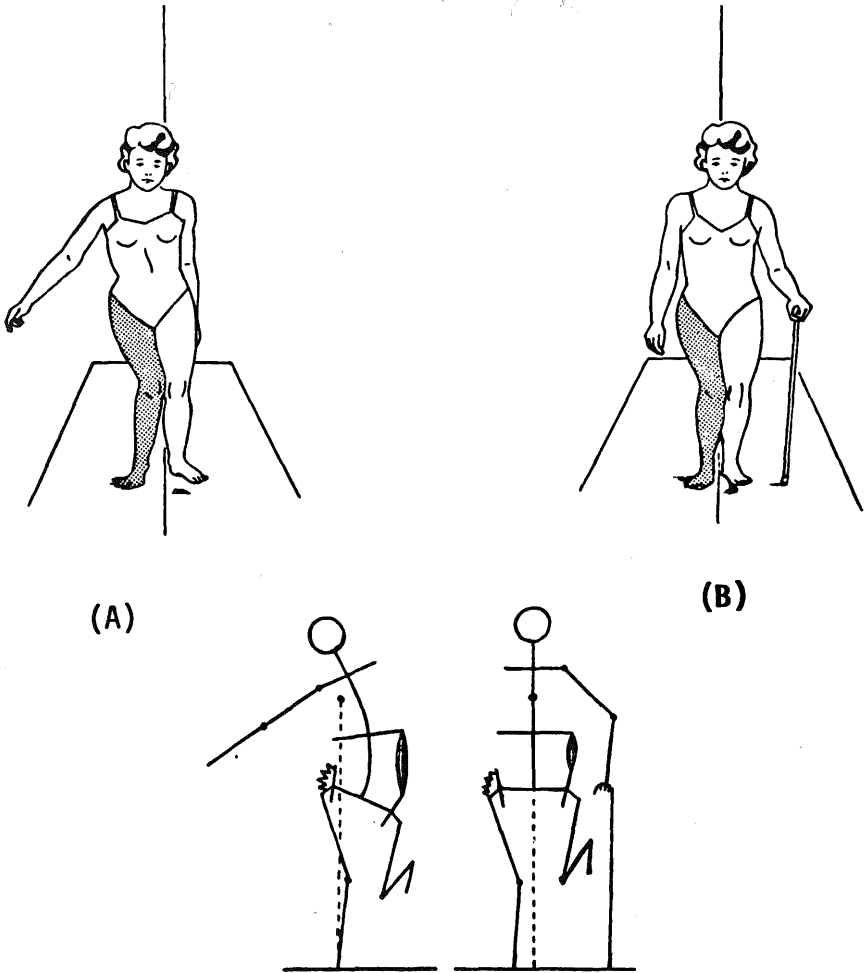


Fig. 5. A) Abnormal motions and forces on the back and knee produced by increased lateral oscillations due to hip abductor muscle paralysis. B) Reduction of abnormal motions and forces achieved using a cane in the contralateral hand.

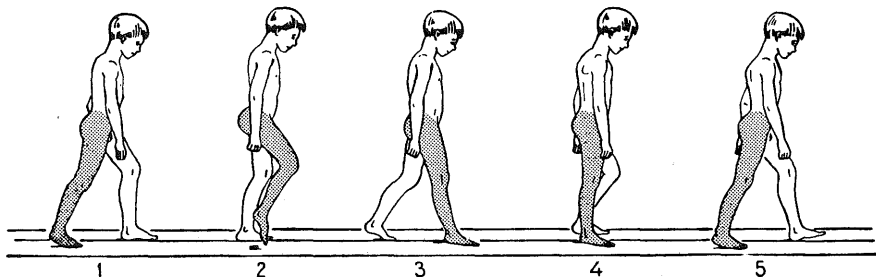


Fig. 6. This boy has paralysis of the dorsi flexor muscles on the right and walks with a drop foot or steppage gait. The excessive hip flexion and forward lean to watch the floor require increased energy expenditure and continuous contractions of the extensor muscles of the neck and back.

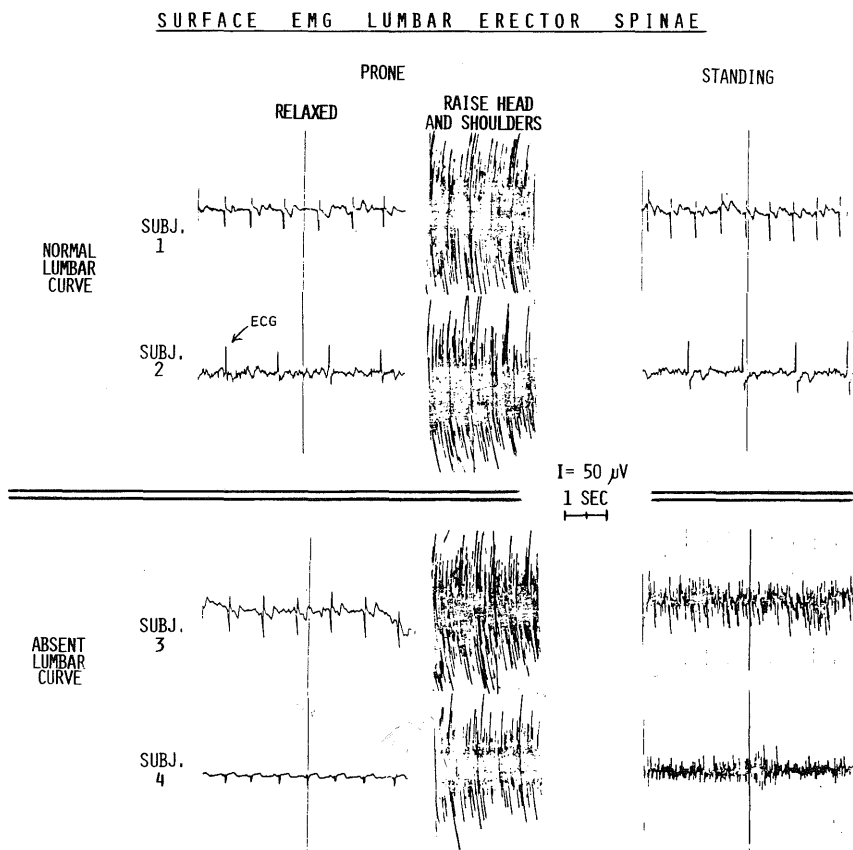


Fig. 7. Surface electrode recordings of electromyographic activity of the left lumbar erector spinae muscles (L3) in 2 subjects with normal postural alignment and 2 subjects with an absent lumbar curve and a slight forward lean. Reference recordings were made in the prone position with the subjects relaxed and raising the head and shoulders to perform the Fair or 3 manual muscle test grade. During habitual relaxed standing, the subjects with normal postural alignment demonstrated inactivity of the lumbar erector spinae, while subjects with absent lumbar curves and forward lean demonstrated continuous low level muscle activity.

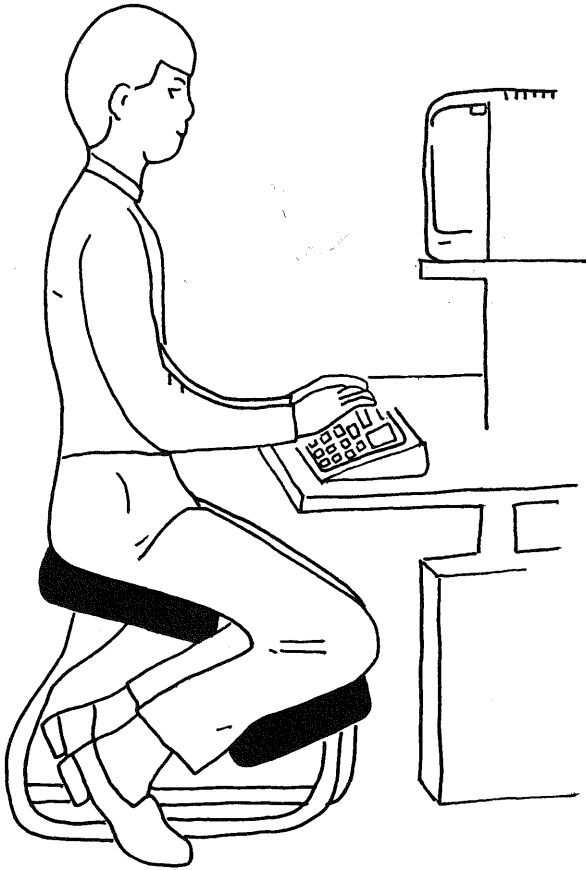


Fig. 8. Balans chair—the forward tilt seat positions the pelvis to foster normal curves.

The objectives for decreasing pain and increasing safety in standing and walking are to 1) improve pelvic alignment, 2) restore weight-bearing capacity of the weaker leg, 3) minimize abnormal gait deviations, 4) increase shock absorption, 5) restore the erect posture, and 6) control unstable or painful joint motions. The methods used frequently serve several of the objectives. Asymmetric pelvic alignment and leg length discrepancies are restored using heel lifts and shoe inserts, which are hardly noticeable compared to the old total shoe elevations. Bilateral weight-bearing capacity is restored by heel lifts, correcting the current orthoses, or applying a below the knee orthosis that controls the knee and ankle (Fig. 9) [6–8].

To minimize abnormal gait deviations and assist weak muscles we first consider shoe variations. The gait of polio patients with calf or dorsi flexor muscle weakness can be improved markedly by placing the ankle in slight

plantar flexion, as in positive heel shoes, cowboy boots, or Swedish clogs (which also provide a mechanical heel rise). The coiled spring dorsi flexor assist is used for dorsi flexor paralysis (Fig. 10) [8, 9]. If there is combined quadriceps and ankle muscle weakness, an ankle-foot orthosis with a 90° perpendicular anterior stop and dorsi flexion spring assist is used to prevent the knee from buckling and provide heel rise and toe clearance (Fig. 9). To reduce lateral trunk deviations, a cane or forearm crutch may be recommended (Fig. 5). Shock absorption can be achieved with microcellular insoles, cushion heels, or crepe soles.

Erect walking posture in the post-polio patient can be regained safely only by removing the need to watch the floor. We recommend boots or athletic supports for ankle stability, the spring wire dorsi flexion assist to prevent tripping, or an ankle-foot orthosis with an anterior stop to provide knee support and control [6]. The woman in Figure 11 has right dorsi flexor and

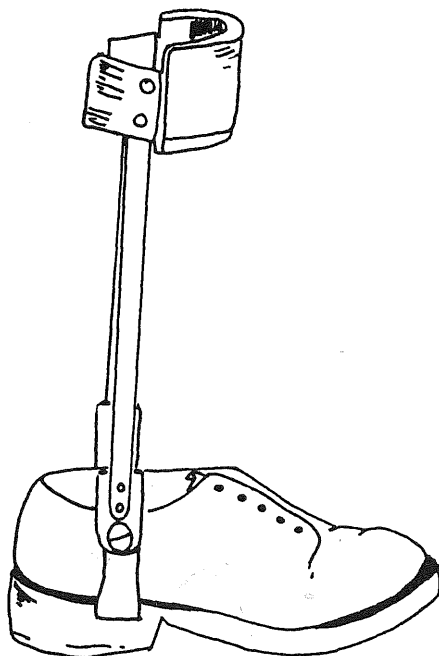


Fig. 9. Example of a type of ankle-foot orthoses used to control knee and ankle motions in gait. The dual channels in the ankle joint accept steel pins or springs. Anterior pins adjusted to prevent the tibia from advancing into dorsi flexion in the stance phase provide quadriceps muscle support. Posterior pins can be used to control hyperextension of the knee in the stance phase, or posterior springs can be used to provide dynamic dorsi flexion in the swing phase. An extended stirrup is required in the sole along with a rocker bottom sole to allow normal gait motions of metatarsal toe break and heel rise.

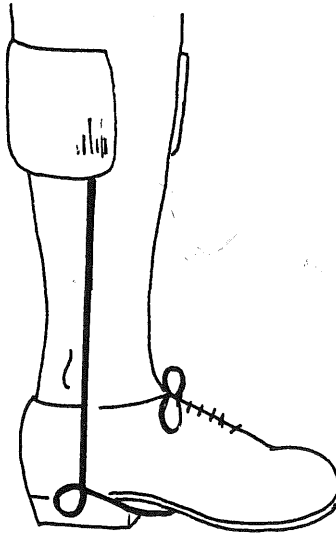


Fig. 10. The coiled spring dorsi flexion splint provides dynamic assistance in the swing phase without limiting motions of plantar flexion in gait or other foot functions such as driving. This splint can be incorporated with positive heel shoes for persons with gastrocnemius soleus paralysis. (The spring dorsi flexor assist produces an increased knee flexion torque at heel strike and therefore requires quadriceps strength.)

quadriceps muscle weakness and previously walked with a drop foot gait and a forward lean. She carefully watched the floor and her foot placement and she was not about to change! Her back and hip pain of a year disappeared after 3 days of using this spring-drop foot assist. She now walks erect, with a more normal gait pattern and with exuberance and well-being.

We have had considerable success in controlling instability and pain in the knee and ankle using the new lightweight athletic knee braces and ankle stirrups or an ankle-foot orthosis. When painful genu recurvatum has been combined with other major weaknesses or instabilities, a knee-ankle-foot orthosis has been required [10].

The upper limb injuries and pain of the long-term crutch walker and user of the manual wheelchair are more difficult to alleviate because of continuous need to use the upper limbs for weight-bearing and locomotion. Rest of the part and avoidance of pain-producing motions are recommended. Medications and physical modalities to decrease inflammation and edema and to promote healing are used as indicated. Mechanical methods for preventing pain and injury are recommended for all persons who use crutches or manual wheelchairs. These include alternative types of crutches to vary the forces, hand grips to avoid point pressure and promote neutral wrist positions, use of lower

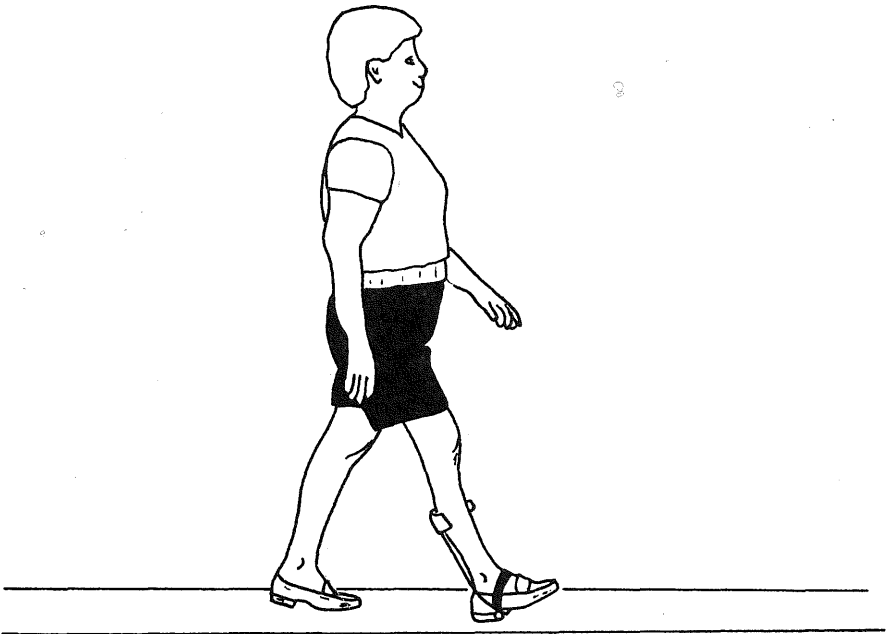


Fig. 11. Use of a coiled spring dorsiflexion assist to minimize abnormal gait deviations and restore the erect walking posture. To compensate for right dorsiflexor and quadriceps muscle weakness, this woman previously walked with a drop foot gait and a forward lean to watch the floor.

limb orthoses to decrease upper limb weight-bearing, and consideration of the new motorized triwheeled vehicles and all-terrain vehicles for distance locomotion.

COMPREHENSIVE PROGRAM

Although corrections of postural abnormalities are sometimes dramatic, in providing immediate pain relief, these corrections are only successful as a part of a comprehensive program. The program requires decreasing nonessential physical activity and exercise, weight reduction, use of energy conservation techniques, modifications of the work and home environment, treatment of inflammatory processes, and provisions for immediate pain relief and control. For example, old surgical sites are sometimes sources of intractable pain. Relief and control frequently can be attained by the post-polio patient using local cold, transcutaneous electrical nerve stimulation (TENS) [11], relaxation techniques, and stretching exercises. This preventive and corrective pain management program requires: 1) identification of medical, social and physical issues, 2) a cohesive team management philosophy, 3) biomechanical

and physiologic evaluation of the causes of pain, 4) demonstrated ability to provoke or relieve pain and to increase function, 5) extensive patient education as to the pathophysiology of acute polio, the recovery process, and the effects of years of compensation, 6) emphasis on cosmesis using modern comforts and technology, 7) provisions of options and alternative means for controlling pain, and 8) time for processing and decision making with support of decisions.

Temporary relief of pain in post-polio is not difficult, but it is an ongoing process of increasing use of medications, physical modalities, inactivity, and decreased function. Pain relief with increased functional ability is possible by a comprehensive program designed to correct the causes and control the sources of pain. The program requires active participation of the post-polio patient. It is not easy and is a challenge for all.

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DISCUSSION

DR. JOHNSON: I noticed that you did not mention two of the things that we see as a common cause of pain, which, if not recognized, can lead post-polios to lose the battle. We see 3 to 6 patients a week, and in the last 6 months, we have seen 2 post-polios with pain due to lumbar stenosis and 6 with cervical radiculopathies. It bothers me that we do not think of pain as a signal, that there is something wrong and look for the cause, as you mentioned in the end.

It is wrong to look for just mechanical causes of what appears to be structural abnormalities, which cause pain that is correctable and more severe.

I do not think you emphasized enough that the body seeks economy of movement. People walk the way it takes the least energy and one must be careful about interposing orthotic devices that may increase energy expenditure.

DR. SMITH: I would agree totally on all points. We have seen post-polios with spinal stenosis, radiculopathies, arthritides, neuropathies, and other known sources of pain. Because of time limits, we did not include these conditions but only addressed presumably postural problems and injury.

Energy expenditure in the body is designed to seek efficiency. If, however, there is an abnormality in gait, be it muscle weakness or skeletal malalignment, increased energy expenditure is required for the task. Most of the time we feel that energy expenditure is decreased using an appropriate orthosis.

DR. FELDMAN: I would just like to make a comment. Frequently, we have found the need to change metal orthoses to plastic ones to reduce the amount of weight that is being transported so as to decrease weakness and fatigue. That in itself sometimes is very beneficial.

DR. SMITH: We have not found that the advantages of the plastic orthoses outweigh many of their disadvantages. The only time weight is a factor is during the swing phase of gait, a relatively low energy phase of gait compared to the stance phase. In the stance phase, we usually need more stability or different types of stability than can be afforded by the plastic orthoses.

DR. PERRY: I think we need to qualify what Ernie Johnson just said, that there is no doubt that the body seeks the most efficient situation for the circumstance at the moment, and if the circumstance is very inefficient, we can improve the efficiency. We have measured energy cost with and without equipment, and very often we have used this as a selling point to the patient who does not like the cosmesis of an orthosis.

I was glad to see use of the double channel ankle-foot-orthoses (AFO) because this provides the rigidity and dorsi flexion stop not provided by the plastic AFO, which is devastating to the quadriceps. One question is why you use a spring dorsi flexion assist rather than a thin plastic shell that is more cosmetic and durable?

DR. SMITH: Probably because we are not familiar with the thin plastic shells. The plastic AFOs we are using are light, but limit motion as compared to the spring drop foot AFOs, which are equally light, do not limit motion, and provide dynamic assistance to the dorsi flexors.

Emotional Responses to the Late Effects of Poliomyelitis

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There has been little systematic evaluation of the process of psychosocial adaptation of people with late effects of polio. The professionals from whom these people seek remediation for new functional and mobility limitations are presented with a range of needs and individual variations that require specialized assessment and treatment skills. Therapeutic regimens and goals sometimes necessitate application of equipment unique to this patient group with which clinical staff have had little or no experience. This information has not been included in most academic or professional training programs, since people with post-polio symptoms have been identified only in the past several years as once again needing medical and rehabilitation services. It is equally important to develop assessment tools and appropriate professional interventions that promote constructive psychosocial and behavioral adaptations.

Over 200 patients receiving rehabilitation services through the Post-Polio Program at The Institute for Rehabilitation and Research, Houston, Texas, were prospectively analyzed to determine the emotional and social consequences of the late effects of polio. The patient group in terms of sex and age (years) consisted of:

- 1.5% males and 1.5% females, ages 20 to 29
- 10.8% males and 18.5% females, ages 30 to 39
- 6.2% males and 23.1% females, ages 40 to 49
- 12.3% males and 13.1% females, ages 50 to 59
- 2.3% males and 6.9% females, ages 60 to 69
- 1.5% males and 2.3% females, over age 70

This evaluation process simultaneously identified those interventions that facilitated integration of treatment modalities, use of mobility aids, change in activity level, and a more pain-free life-style by the person and family. The emotional responses of the patients with post-polio sequelae were found to be related to the: 1) severity of the newly felt functional limitations; 2) impact on social role due to chronologic age at time of onset of the late effects of polio; 3) coping patterns that were established during the person's

recovery from the acute onset; and 4) the support systems that were and are now available to the person and family for participation in the community.

The range of emotional and intellectual attributes that a person with post-polio concerns brings to the professional when seeking remediation will be identified and described. It is hoped that this labeling process will serve as an assessment and treatment guide for the emotional and social consequences of the late effects of polio.

BEHAVIOR PATTERNS

Most of the people seeking restorative services were already experiencing, or anticipating, the collapse of their abilities (mental, emotional and/or functional). Many had sought relief previously only to have had their own assessments of these deteriorating conditions discredited by other professionals. It became obvious that any recommended change resulted in a sense of loss for the "usual" way of functioning. It is the person's definition of that loss, not the professional's, that determines how much emotional energy the person must harness and then generate in order to push themselves into that change. In order to better assess a person's capacity for change, it was necessary to identify their general *personality styles* and the types of coping mechanisms that were usually employed to deal with life. Was the person manic-depressive, thus experiencing wide mood swings apart from a frustration response to uncontrollable physical weakness and fatigue? Was that a behavior pattern of the past 20 years or only since the onset of the post-polio symptoms?

Did the person display an obsessive/compulsive nature that ritualized all daily activities? Depending upon the symbolic significance for which a particular series of behaviors had to occur, there would be greater or lesser resistance to change. Associated with this personality style was a perfectionistic approach to any activity. Certain tasks could only be executed in one precise manner. Little room for creative thinking existed, and listing of options or delegation to others could not be tolerated. It was either the right or the wrong way, and it would be demeaning to function differently. People who approached life in this manner tended to project the problems and lack of solutions onto others. Although this trait is exhibited by intellectually competent people, it is imperative that a person's cognitive abilities not be construed to equal their capacity for change. The majority of the alterations that were and are being suggested require emotional accommodations to unwanted changes.

The presence of *pain* was also an indicator of change in social interactions. Those people with chronic pain described diminished memory and problem-solving abilities, which impaired productivity at work and construc-

tive family relationships. These negative consequences of the pain often created long-lasting effects that required therapeutic interventions following successful resolution of the primary causes of pain. It was necessary to treat the pain condition first in order to redirect the energy that had been used to defend against the pain toward repairing familial relations.

Closely associated with pain problems was the presence of *sleep disorders*. The lack of restful sleep stockpiled feelings of fatigue, weakness, and pain, which impaired mental and emotional processing, decreased frustration tolerance, and lowered impulse control. It also resulted in unpredictable energy levels, which allowed them to do certain activities but not on a regular basis. Family members had difficulty understanding this and felt that they were being manipulated.

These behaviors placed stress on *marital relationships*. The durability and longevity for that familial system is determined by the communication style, emotional bonding, and external support network that previously and currently exist. It was also important to evaluate the *parent-child* and *sib relationships* that existed after the person recovered from polio. The majority of people described exceptionally supportive and loving families. However, some people reported intense feelings of anger that they instead of a sib had contracted polio, which impaired that relationship throughout their childhood. Others felt that the dependency they had upon their parents because of the polio had slowed the process of separation and individuation.

Another response was that their sense of difference was never fully acknowledged, since the major emphasis was on mainstreaming and proving that they were as capable of doing and accomplishing things as well as, if not better than, others. Many people attributed their academic achievements to this attitude and acknowledged both its positive and negative aspects. For some people, learning was not an easy task; it was most difficult for them to compensate intellectual mastery for physical impairments. It was also stressful to be encouraged to discard mobility and gait aids, which allowed the individual to function more comfortably but came to represent the lack of a cure if they continued to be used. Some people in their 40s and 50s openly stated that any new cane, crutch, or brace would only be used when they were not with their parents for fear of the aids being destroyed. Similar was the feeling of "unfair" competition with able-bodied sibs and friends in any sports activity. The difference in physical body form, strength, endurance, and coordination was never acknowledged openly. Positive feedback was absent for having had to take more risk or expend more energy to accomplish the same task. Some felt that they were asked to deny that they were physically different. For those who were able to "pass" as normal, it was all the more traumatic to have their body "quit" on them and make them face limitations. Some people described developing a dread of vacations because of how tired

and painful their bodies would feel. Some of these feelings were still strong and unresolved, although they could be verbalized. These attitudes sometimes spilled over into their current marriages and work relationships. When constructive interactions did not exist, it was important to identify them as a goal for remediation apart from medical and physical ones.

Addictive behaviors presented yet another challenge to ameliorate in order to maximize functional abilities. Many people who had been chain smokers for the past 20 years were now experiencing respiratory, cardiac, and circulatory difficulties. Still they were not yet ready, willing, or able to stop smoking! Similar problems existed with alcohol consumption and abuse of pain medications. Some people required referral to treatment programs for their specific addiction. This was also true for people with *eating disorders*, since a determination had to be made about referral to a weight reduction program. Would that be sufficient or did the obesity stem from an underlying lack of self-esteem that required additional counseling in order to obtain the desired weight loss? Any of the recommendations made by the professionals had to be presented in a fashion matched with the person's needs and capacity for change. Seemingly innocuous suggestions, such as to avoid wearing high heels, going for a walk at lunch time, standing at social functions, or sleeping curled in your spouse's arms, required them to develop a new self-concept of how their new bodies were going to allow them to function. Given the wide range and uniqueness of the residual impairments due to the polio virus, each of the suggested treatments had to be individualized and monitored at intervals to determine if the desired goals were being obtained. This created an uncertainty about prognosis at the same time that the goals clearly stated that a reduced level of activity would permit maintenance of the current functional level within pain-free limits. The goals often were not aimed at a return to the prior level of functioning over the past 20 to 30 years. This double message had to be openly acknowledged since the feelings of strangeness and insecurity must be counteracted if a trusting relationship were to develop and be maintained.

EXPECTATIONS

Almost universally, there was an expectation for a "cure" for all of the symptoms that were being experienced. Now that the medical community was finally legitimizing their complaints, they would and could have their previous life-styles restored. If the professionals were listening and taking them seriously, then surely research monies that in the past had produced the polio vaccines were being refocused on polio. It could not be possible that medical science would fail them a second time! Some were even surprised that monies were not available to pay for the medical and therapy evaluations or

equipment, since many had received full sponsorship through the March of Dimes during their acute episode. This orientation resulted in double disappointments and made incorporation of new information even more difficult.

Extinguishing all pain was also expected to be possible. One right medicine or exercise regimen would accomplish this without any alterations on their part. If the professional could not provide this, then the professional was labeled as incompetent or unwilling to listen.

The total aim was to *regain lost strength*. Many people demanded strengthening exercises, even though they had already tried them on their own or under other professional supervision without achieving the desired success. They believed that the recommendations should be aimed only at a return to the *previous functional level*. Some would consider reducing their activity level for a short period of time with the prospect of accumulating enough energy to rebuild to previous levels. The concept of maintenance versus progression was resisted by most.

They preferred *no modification* in their sitting, walking or sleeping positions; delegation of tasks; work place; retirement and/or travel plans. When people were confronted with information they did not want, the problems were externalized to others for a period of time, until their expectations could be reoriented. The scheduling of follow-up appointments provided the time in which this reorientation process could occur.

DYSFUNCTIONAL ASSUMPTIONS

The process of recovery from acute polio required the development of certain attitudes and behaviors. The movement from loss of function to restoration of function was achieved only through focusing on a goal rather than on the effort that was being expended at the time. In this way, *hard work* came to be the "cure" for polio. People had to learn to disregard the pain feedback mechanisms of the body in order to gain function. The opposite behavior is now being asked of them. They are being taught to tune in and listen to the body's pain response as a means of avoiding more pain, muscle cramps, weakness, and fatigue.

Physical activity was the only means to regain strength in the acute phase. Thus, physical activity came to be equated with strength, so that any decrease in it caused the person to further increase their activity level in hope of becoming stronger. Often the opposite happened, since a cycle of reinforcing weakness began.

Increased strength had been described as the ultimate goal of therapy. If a task could be performed again, that was equated with being stronger. There was little differentiation among strength, endurance, and function.

To be able to discard *adaptive equipment* became another goal for some.

It was unrelated to basic body mechanics and an understanding of the residual impairments.

Due to all the praise and personal gratification for functional accomplishments, people began to believe that their *productivity determined love and acceptance*. Their sense of goodness and self-worth were defined by how well they felt they had produced. When it is suggested now that they produce less by curtailing their energy output, a sense of worthlessness emerges. Depending upon the intensity of the fusion of productivity with love, in the person's mind, a great fear of abandonment and loss of love also occurs. This response usually requires supportive therapy because of its origin in childhood. All of these suppositions must be compensated for now with intensive reeducation to facilitate the formation of constructive assumptions.

LIFE-STYLE CHANGES

To create life-styles conducive to living with the late effects of polio, it became evident that certain perceptions required expanded definitions. The person's view of *activity level* needed to incorporate a sense of quality in addition to quantity. If there were only the memory of pain and exhaustion, devoid of any sharing and sense of well-being, then perhaps the activity or series of activities was really not meaningful after all. The focus needed to shift to the process and consequences, not just the fact that the task had been completed. If socialization were desired, it could occur in the person's home with the guests providing the food. It did not mean that after a work week, the person had to market, houseclean, prepare the dinner, and clean up. Education about cumulative energy expenditure was found to be the most helpful in modifying their demands on their bodies.

Language creates symbolic images, which influence the positive or negative views that people hold of themselves and others. The difference in comfort level in saying "*limitations*" instead of "*disability*" was enormous. For many people, their functional style was normal, and they had managed to find a way to do and participate in whatever pursuits they wished. It is important to note when the term "*wished*" is used, since many people closed off from their consciousness those activities that would pose problems. Therefore, they did not define themselves as disabled. Even in defining the new loss in functioning, many still used the term "*limitations*" rather than "*disability*." It is important to flow with the language that is most comfortable for the person instead of confronting the issue and possibly adding another emotional stress. Merely presenting someone with an application for a handicapped sticker was enough to close off hearing about other recommendations that might have been tolerable. After a strong patient/staff relationship

has been established, it might be worthwhile to discuss the symbolic nature of these words.

The use of *adaptive equipment* also held great symbolic meaning, which had to be acknowledged to enable the person to try to incorporate them into a new body image. Several people reported purposely sabotaging the use of a shoe lift, cane, or orthosis because it showed the world that they were disabled. This was most stressful for people who had never even told others that they had contracted polio. Often it was necessary to provide information in a sequential manner to allow the person to identify the benefits or experience the pain to the point that they knew they had to change their perception.

Support systems have always played a primary role in adapting to polio, although support may have been restricted to the family or a small group within the same community. There was also the backing of the entire nation for medical care, research, and entry into local schools. The information sharing has continued through the efforts of the Gazette International Networking Institute and now the emotional sharing is emerging in the form of support groups around the world. For many people, reading the books and attending the meetings was easier than identifying those people from whom they would ask and accept assistance. They had fought so hard to gain every inch of independence that to develop dependency or interdependency relationships signaled failure. Timing of referral and active participation in support groups should be when the person's capacity for learning has emerged and there is sufficient energy to grow. The distance, location, and transportation arrangements also need to be evaluated so that additional energy demands are not placed upon the person.

BEHAVIORAL CHANGE TECHNIQUES

Some people reported feeling overwhelmed by all the functional and life-style changes they had to "newly" master. The following techniques were developed by pooling insights from patients, their relatives, and the multidisciplinary staff at the Institute for Rehabilitation and Research. The focus was on providing people with tools they could easily implement and facilitating their ability to change.

The *push to avoid pain* system acknowledges the amount of energy that must be generated in order to reduce one's activity level. It is a statement of action, not of failure or backing down. It means that the person is dedicated to taking care of him or herself. Other people, obligations, and commitments will be prioritized according to pain thresholds and those actions that reduce pain. To delegate is action; to use nighttime oxygen or respiratory equipment is an action with enormous consequences; to retain authority in a seated position

requires great assertiveness. To take care of oneself is not giving in but rather a restatement of control. The pain will not control the person; the person will control the pain.

The *blank pad* method of documenting accomplishments during the day has reinforced a sense of purpose. Instead of making list after list of things to be done and then crossing off what has been completed, people are instructed to use a blank pad to record all that they have done. It is a great training exercise for developing awareness of all the energy expenditure that does occur. It also saves the person from devaluing himself for that which was not accomplished. The goal is to avoid negative feedback at the end of the day and replace it with positive feedback.

Plain talk was developed in response to people asking how to keep themselves and others from feeling manipulated. The person simply asks, "Why do you want me to be in pain, more tired, overextended, not able to enjoy our time together, etc?" People need to practice simply worded questions that will increase the other person's awareness of the impact of their request without creating defensiveness.

SUMMARY

It is necessary to identify and analyze the unique psychosocial stressors that may be impacting on a person with post-polio syndrome to facilitate their incorporation of medical and rehabilitation recommendations. It is hoped that the information presented will be used to increase the awareness of the range of emotional responses that people with late effects of polio may have to enable staff to establish sequential presentation of information and guidelines for changes in energy output and life-style patterns. The suggested interventions are given with the aim of facilitating more rapid integration of treatment regimens that will lead to a better quality of life.

DISCUSSION

DR. SPROTT: One of the things that intrigues me, to which you alluded slightly in part of your presentation, was the number of these people who felt that they had to remain productive in order to remain loved and so on. Your talk implies that that behavior may be irrational. To what degree is it not irrational? How many of the families in fact push the patient and will treat them differently if the family views their activities as giving up?

DR. KOHL: Let me start from the other side. The person who bases their self-identity and self-worth on what they produce as the only aspect of their life that has value builds a self-definition on a void. They do not have multiple building blocks for their self-worth. If you feel good about yourself because

you have grown up in a secure family, and there were other attributes that were valued, you have an intrinsic self-worth separate from what it is you produce, either in school or professionally, when someone then suggests that you do not produce enough, it does not shake your self-image and self-definition. I think that the majority of families did a lot of pushing because they thought it was the best way to help people to be mainstreamed. A lot of people do credit their families for that push and the support for their success. Some of the families then would feel very comfortable in supporting people to do less. There were a few families, however, where that indeed was a real problem for the individual. The majority of families were much more supportive than the individual was willing to give them credit for, and it was more the patient's difficulty of equating the loss of their productivity with a diminished sense than the perception of the family members.

DR. SPROTT: Relative to your statement about the support groups, I guess my experience has been that I agree with you on one level—that certainly a support group is not appropriate for everyone, and there definitely are people who need individual counseling at different levels, including psychiatric. On the other hand, on a general basis, I think that the support groups have been as beneficial as many professionals could be with the same amount of time because one advantage of support groups is that it does happen slowly.

DR. KOHL: I was referring to the damage to the support group system by the individual who enters the group and drains the energy from that support system. I was suggesting that as professionals, we should help the patient be directed to other professionals to obtain the help that they need. We have had several people who have either become suicidal, or they bring all of their family problems to the support group for solutions. The support group gets drained, and it is not permitted to perform its important service and function of sharing information and reinforcing people's ability to change and adapt.

Stress and “Type A” Behavior as Precipitants of Post-Polio Sequelae: The Felician/Columbia Survey*

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A behavioral profile has begun to emerge from studies of persons who survived acute poliomyelitis and are now experiencing post-polio sequelae. Persons who had polio have been shown to be employed full time at four times the rate of the general disabled population [1, 2]. Persons who had polio have more years of formal education on average than the general population [3], and marry at approximately the same rate as those who are not disabled [4]. These data, combined with our own experience with thousands of persons who had polio, indicated that “polio survivors” are competent, hard-driving and time-conscious overachievers who demand perfection in all aspects of their personal, professional, and social lives. It appeared that those who survived polio exhibit “Type A” behavior and would therefore experience chronic emotional stress.

The notion that individuals who had polio exhibit “Type A” behavior and experience chronic stress was thought to be extremely important for an understanding of the pathophysiology and treatment of post-polio sequelae (PPS). Animal studies have demonstrated that stress accelerates the onset of muscle fatigue [5], augments age-related decreases in the terminal axon branch number [6], and accelerates age-related losses of neurons [7]. Therefore, this study was designed to test 2 hypotheses: 1) persons who had poliomyelitis exhibit “Type A” behavior and symptoms pathognomonic of chronic stress, and 2) “Type A” behavior and stress precipitate or exacerbate PPS.

METHODS

The Felician/Columbia Survey

In order to test the above-stated hypotheses, a self-administered survey was designed to record demographic data, quantify “Type A” behavior,

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document psychophysiologic symptoms that are recognized as concomitants of chronic stress (including disturbed sleep), and identify the conditions that precipitated or exacerbated PPS.

Quantification of "Type A" behavior. To quantify "Type A" behavior, the Young and Barboriak brief "Type A" questionnaire [8] was included as part of the survey. This instrument consists of 10 questions that elicit responses characteristic of "Type A" behaviors and attitudes (Table 1). It was tested by its authors on a sample of nondisabled males (mostly professional or paraprofessional hospital employees) who were employed full time and who were without cardiovascular disease. They obtained a mean score of 35.6 (± 14.0) for this control sample, and 80% agreement was found between their brief "Type A" score and that obtained using the 65-question Jenkins Activity Survey.

All "Type A" questionnaires, including the Young and Barboriak instrument [8], are designed to quantify the behavior of men who are employed full time outside of the home. Since the post-polio population includes men and women, some of whom are employed part time, in the home, unemployed, or receiving social security disability, it was recognized that some of the post-polio respondents would not be able to complete all 10 questions. Therefore, the scoring of the Young and Barboriak questionnaire [8] was modified in consultation with its authors. It was decided that all questionnaires would be scored by assigning 10 points to each "Type A" response, summing those responses, and dividing by the total number of questions answered. This provided a "Type A" percentage on the basis of 10 questions, in persons who were employed full time, and on the basis of 7 questions (eliminating questions 2, 5, and 8) in persons who were not employed full time. The 7-question "Type A" score has been found by the authors of the questionnaire to correlate well with the 10-question score (Young, personal communication).

TABLE 1. Brief "Type A" Questionnaire

1) Do you usually wake up in the morning not feeling well rested?
√2) Do you enjoy competition on the job?
3) Do you consider yourself "hard driving?"
4) Do you have a temper that is hard to control, fiery?
√5) Do you have at least one deadline per day on your job?
6) Do you set at least one deadline each week for yourself?
7) Is it very important for you personally to get ahead in life?
√8) Do you spend more than 8 hours a week doing overtime work at home?
9) Do you usually spend less than 5 days on an average vacation?
10) Have you taken less than one vacation per year during the last 5 years?

√ = Questions omitted in respondents who are not employed full time.

Documentation of psychophysiologic symptoms. To document the occurrence of psychophysiologic symptoms that are recognized as concomitants of chronic stress, subjects were asked if they experienced frequent feelings of anxiety, headaches, muscle spasms, and "difficulty in falling asleep because the mind is racing." They were also asked if they had been diagnosed as having asthma, hypertension, coronary artery disease, ulcer, or colitis. In addition, subjects were asked if they were experiencing "generalized random myoclonus" (GRM), the slow contraction and rapid twitching that occur randomly in limb and trunk muscles during sleep and especially at sleep onset [9]. They were also asked if their sleep was disturbed by GRM.

Psychologic stress and other precipitants of PPS. Subjects were asked whether emotional stress or "upset" precipitated or exacerbated the 3 most frequently reported and least well understood PPS—muscle weakness, muscle pain, and unaccustomed fatigue. They were also asked if these symptoms were precipitated or exacerbated by physical overexertion, exercise, or exposure to cold and hot ambient temperatures. Finally, the subjects were asked if PPS interfered with their ability to participate in social activities, complete or perform work, and perform self-care activities; they were also asked about their attitudes concerning their new symptoms and the general topic of disability. (Functional and attitudinal data will be presented elsewhere.)

PROCEDURE

Distribution of the Survey

On April 1, 1985, 1,200 surveys were mailed to all self-identified post-polio clinics and support groups in the continental United States. Respondents were instructed to complete the survey after April 15 and to return it by June 30, 1985. A copy of the survey was obtained by a national organization that provides services for persons with disabilities. The organization reproduced the survey and mailed it to their offices across the country for distribution without our knowledge. While this unexpected distribution probably increased the number of persons who obtained the survey, control of the sample was lost and no meaningful response rate can be reported.

Surveys that did not include a completed "Type A" questionnaire or reported a co-existing medical condition that could cause muscle weakness, muscle pain, or fatigue (eg, arthritis, cancer, CVA, hyperthyroidism) were not included in the analysis.

Data Analysis

Orthogonal analysis of variance and independent groups *t*-tests were applied to compare parametric variables between groups. The chi-squared

statistic was applied to compare the frequency of nonparametric variables between groups. A value of $P < 0.05$ was considered statistically significant.

RESULTS

Demographics, New Symptoms and Level of Functioning

The respondents were remarkably similar to those in other surveys of persons who had polio (Table 2). The average respondent was a 52-year-old female, who had acute poliomyelitis in 1948 at age 10.5 years. She was experiencing unaccustomed fatigue, muscle weakness (in muscles originally affected by the polio), and muscle pain. She ambulated without orthotics or ambulatory aids prior to developing new symptoms but required some assistive device (brace, cane or crutches) with the onset of PPS (Table 3). It should be noted that the ability to ambulate distinguishes these respondents from those in other surveys. The percentage of respondents who ambulated unassisted prior to PPS was 1.4 times *greater* than in other surveys. The percentage who used ambulatory aids or a wheelchair either prior to or following PPS onset was at least 2 times *less* than in other surveys.

TABLE 2. Comparison of Demographic and New Symptom Data From Surveys of Persons Who had Poliomyelitis and are Experiencing PPS

Demographics	Post-Polio Surveys		
	Felician/Columbia Survey	Halstead et al [10]	Halstead and Rossi [11]
Number of Subjects	676	201	539
% male	32	32	41
% female	68	68	59
Current Age:			
mean	52	50	53
median	51	49	53
range	58	52	68
Years since acute polio:			
mean	41	38	37
median	37	34	34
range	77	54	67
Year of acute polio:			
median	1948	1949	1949
range	77	54	67
New Symptoms (% of subjects)			
Muscle weakness in muscles affected by poliomyelitis	82	82	87
Muscle weakness in "unaffected" muscles	44	71	77
Muscle pain	76	76	80
Fatigue	91	87	87

TABLE 3. Comparison of Ambulatory Aid and Wheelchair Use Data From Surveys of Persons who had Poliomyelitis and are Experiencing PPS

	Post-Polio Surveys	
	Felician/Columbia Survey	Halstead et al [10]
Use of ambulatory aids or wheelchair (% of Subjects)		
Used NO aids or wheelchair:		
before new symptoms	61	44
after new symptoms	44	40
Used ambulatory aids:		
before new symptoms	25	56
after new symptoms	30	60
Used wheelchair:		
before new symptoms	14	40
after new symptoms	26	59

“Type A” Score in Post-Polio Subjects

The mean “Type A” score for all respondents was 53.2 (± 21.7). This score was significantly higher ($t = 8.10$; $P < .001$) than the 35.6 (± 14.0) reported by Young and Barboriak [8] for their nondisabled control sample. The “Type A” score in each post-polio subgroup, whether or not PPS were reported, was significantly higher than the control score of 35.6 ($P < .001$) (Figs. 1–4).

“Type A” Score, PPS and Psychophysiologic Symptoms

Between 88% and 91% of the respondents reported new decreases in muscle strength, increased muscle pain, or new or increased fatigue. The “Type A” score was significantly higher in respondents reporting muscle pain

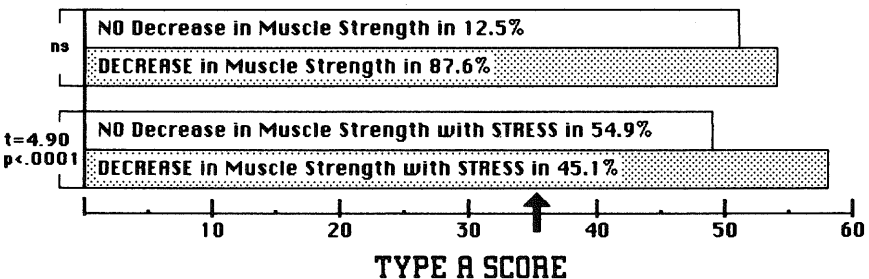


Fig. 1. Decreased muscle strength. Comparison of “Type A” scores between subjects with and without “new decreases in muscle strength” and decreased muscle strength following “emotional stress or ‘upset’.” In all figures, the percentage of subjects reporting symptoms is given inside each histogram bar. The control “Type A” score of 35.6 (at arrow) is significantly lower than the “Type A” score in any post-polio subgroup.

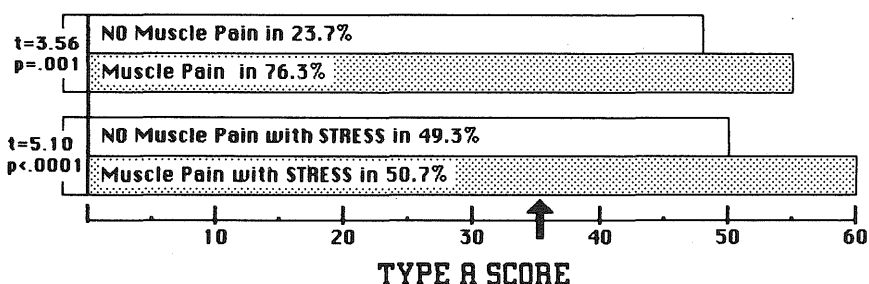


Fig. 2. Muscle pain. Comparison of "Type A" scores between subjects with and without "new muscle pain" and muscle pain that occurs or increases with "emotional stress or 'upset'."

and fatigue (but not decreased muscle strength) as compared to subjects without these symptoms (Figs. 1–3).

Symptoms pathognomonic of chronic stress were reported by 49% to 58% of the respondents (Fig. 4). The "Type A" score was significantly higher in subjects who reported these psychophysiological symptoms than in those who did not.

GRM was reported in 32.8% of the respondents and 29.9% reported both GRM and that their "sleep was disturbed by muscle twitching." It is noteworthy that there was *no* relationship between GRM or GRM-disturbed sleep and reports of daytime fatigue.

Stress and Other Precipitants of PPS

"Emotional stress" was the *second* most frequently reported cause of fatigue (61% of respondents) and the *third* most frequently reported cause of decreased muscle strength and muscle pain (45% and 51% of respondents, respectively) (Fig. 5). The "Type A" score was significantly higher in subjects reporting that their symptoms were exacerbated by emotional stress as compared to those who were unaffected by stress.

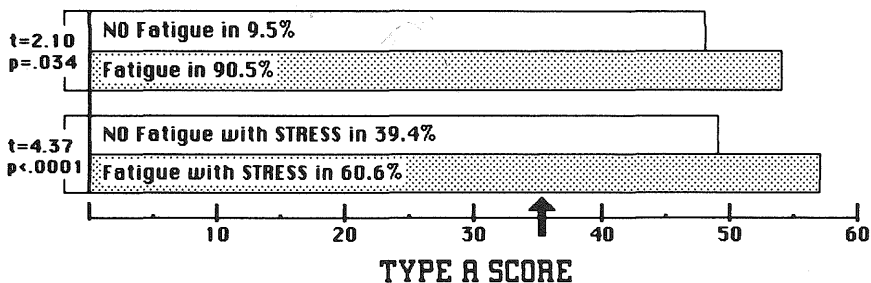


Fig. 3. Fatigue. Comparison of "Type A" scores between subjects with and without "new or increased fatigue" and fatigue that occurs or increases with "emotional stress or 'upset'."

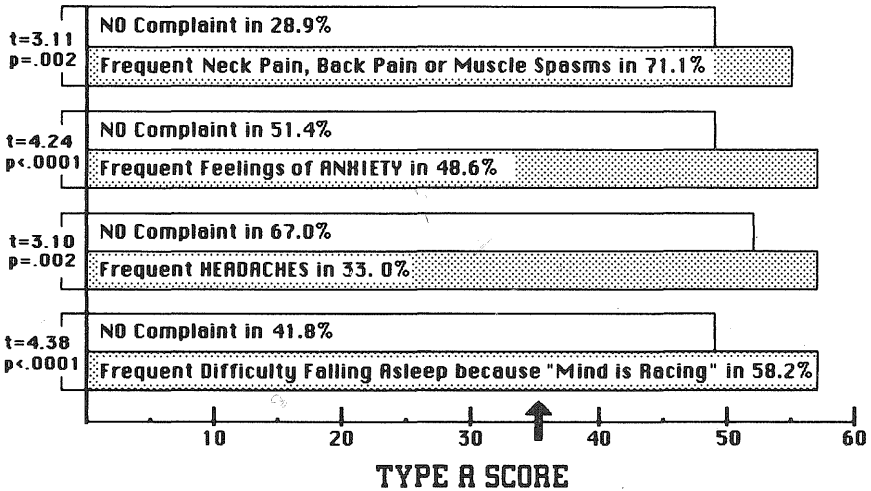


Fig. 4. Psychophysiologic symptoms. Comparison of "Type A" scores between subjects with and without psychophysiologic symptoms pathognomonic of chronic stress.

Exposure to cold ambient temperatures was the *second* most frequently reported cause of decreased muscle strength and muscle pain (62% and 60% of respondents, respectively). Exposure to cold or to heat was reported by 39% of the respondents as the *third* most frequently reported cause of fatigue. As in all other studies, the most frequently reported cause of decreased muscle strength, muscle pain, and fatigue was physical overexertion or exercise (reported by 92% to 95% of respondents).

DISCUSSION

The data indicate that both hypotheses should be accepted: 1) persons who had poliomyelitis demonstrate significantly more "Type A" behavior than do nondisabled controls, and evidence psychophysiologic symptoms pathognomonic of chronic stress, and 2) PPS are initiated or exacerbated by stress. In addition, there is an interrelationship between these 2 hypotheses. "Type A" scores are significantly higher in respondents who report that stress initiates or exacerbates PPS and in those subjects reporting psychophysiologic symptoms, new muscle pain, and unaccustomed fatigue.

Genesis of "Type A" Behavior in Persons Who Had Polio

There are a number of hypotheses as to why persons who had poliomyelitis exhibit "Type A" behavior and experience symptoms of chronic stress. It is possible that adults and even children who exhibited "Type A" behavior and were experiencing stress were more susceptible to infection by polio viruses

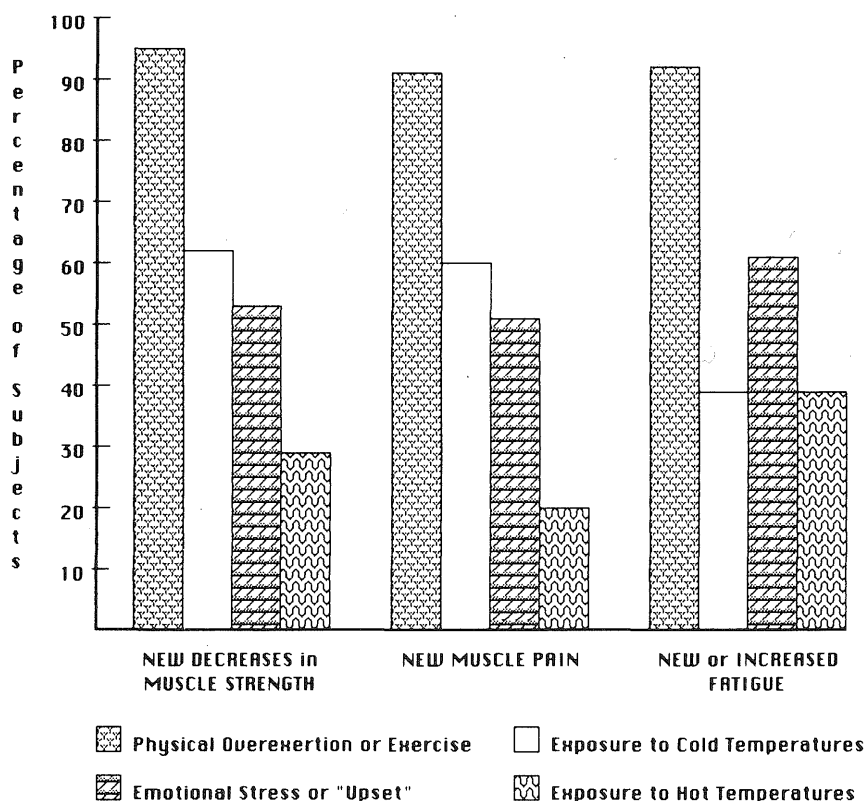


Fig. 5. Correlates of new symptoms. Percentages of subjects reporting new decreases in muscle strength, new muscle pain, and new or increased fatigue following "physical overexertion or exercise," "exposure to cold or hot ambient temperatures," and "emotional stress or 'upset'."

because of stress-induced immunosuppression. It is also possible that to survive the acute polio infection and then thrive despite paralysis in a totally inaccessible world, the special drive of the "Type A" personality was required. It might also be the case that persons with disabilities must learn "Type A" behavior in order to succeed in a "barrier-full" society. For example, physical limitations might require one to become "time-conscious" to perform common tasks that require more time to complete than for persons who are not disabled. Social prejudice might require persons with disabilities to become "hard-driving overachievers"—personally, professionally, and especially physically—to be accepted by peers and employers.

This last hypothesis raises the question as to whether orthopedically disabled persons in general, but especially those disabled early in life, exhibit "Type A" behavior, experience chronic stress, and may also have late-onset

TABLE 4. Comparison of Data From the Felician/Columbia Survey and From a Survey of Adults With Spina Bifida Who are Experiencing New Symptoms

Demographics	Felician/Columbia Survey	Dunne, Shurtleff, Gingher and Olsen (Spina Bifida) (Personal Communication)
Number of subjects	676	285
% male	32	32
% female	68	68
Current age (% of subjects):		
<40 years	19	69
≥40 years	81	31
Years of education: mean	15	13
Ambulation and use of ambulatory aids or wheelchair (% of subjects)		
worsening ambulation	26	32
used NO aids or wheelchair	44	33
used ambulatory aid	30	39
used wheelchair	26	28
New symptoms (% of subjects)		
muscle weakness	88	40
muscle pain	76	0
joint pain	79*	48
fatigue	91	0
hypertension	29	15

*Data from Halstead and Rossi [11].

problems. A recently completed study has identified late-onset problems in adults with spina bifida who, although younger than the post-polio population, are similar in educational level and ambulatory ability (Table 4) (Gingher, personal communication). It is interesting to note that muscle weakness, joint pain, and hypertension were reported about half as frequently in the spina bifida sample as in persons who had polio, while fatigue and muscle pain were not reported at all. We are presently conducting a survey of adults with spina bifida to document "Type A" behavior, psychophysiologic symptoms, and late-onset problems.

Stress and the Pathophysiology of PPS

The mechanism whereby stress induces or exacerbates PPS has not yet been described. Stress in animals has been shown to cause a variety of abnormalities that may contribute significantly to the pathophysiology of PPS. Stress has been shown to accelerate the onset of muscle fatigue and shorten life-span [5]. Stress has also been shown to augment age-related decreases in the number of terminal axon branches innervating both hind-limb and diaphragm muscles [6]. A decrease in the number of functional terminal axon branches may be responsible for the shrinkage of motor unit territories

seen in persons who had polio [12] and has been implicated as a probable cause of post-polio muscle weakness [13, 14].

Corticosterone secretion, a specific hormonal concomitant of stress, has been shown to have deleterious effects that directly relate to the hypothesized pathophysiology of PPS. Elevated corticosterone levels have been associated with the inhibition of axonal sprouting in aged animals with motor neuron denervation [15]. Further, stress-induced hypersecretion of corticosterone has been shown to accelerate age-related losses of hippocampal neurons [16]. This effect is thought to result from corticosterone-induced inhibition of neuronal glucose uptake and the impairment of neuronal energy metabolism in these "metabolically vulnerable" neurons [7]. It has been suggested that polio-damaged and extensively sprouted anterior horn cells are also metabolically vulnerable, and that post-polio muscle weakness might occur as these neurons fail to function and even die because they "are just not able to keep pace with the metabolic demands of innervating all of their muscle fibers" [13]. Clearly, research needs to be conducted to document the relationship between the physiologic effects of stress and the pathophysiology of PPS.

Clinical Implications

This survey has documented the deleterious effects of physical overexertion and exposure to extremes in temperature in persons who were less severely affected by the original polio infection than were subjects in other studies [10, 11, 17]. It has also documented that GRM occurred in nearly two-thirds of this post-polio sample. However, the failure to find a relationship between GRM-induced sleep disturbance and daytime fatigue suggests that GRM may not be a contributor to new and unaccustomed fatigue.

Most importantly, this survey demonstrated that emotional stress is a precipitant of PPS. Fortunately, it is a precipitant that can be treated. Post-polio clinics and support groups should include stress management as an integral part of both therapeutic and wellness programs. We are presently studying combinations of cognitive and autonomic stress management techniques designed to reduce "Type A" behavior, counter the psychophysiologic symptoms of stress, and thereby decrease the symptoms of post-polio sequelae.

ACKNOWLEDGMENTS

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The Impact of Life Support Technology Upon Psychosocial Adaptation to the Late Effects of Poliomyelitis*

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INTRODUCTION

This paper examines the impact of changes in respiratory support technology upon the quality of life and current experience of aging effects among a selected sample of ventilator-dependent people. Data were collected during a follow-up study of survivors of the major Manitoba poliomyelitis epidemics of the 1950s [1]. The project included an audit of medical records from the time of the epidemics and 2 surveys: one tracing and interviewing people with respiratory paralysis requiring mechanical ventilation and a multimethod survey of nonrespiratory cases who had been admitted to the same hospital at the time of the epidemics. In addition, a series of in-depth interviews was conducted over an 18-month period with 10 of 29 individuals who continue to be fully or partially dependent upon mechanical ventilation.

Our objective was to combine this qualitative or life historical data with the results of the epidemiological analysis of the total population to provide a more complete understanding of aging and adaptation among those who have lived through these experiences. The subjects studied in depth were selected on the basis of their use over time of a variety of methods of mechanical respiratory support. The interviews explored different dimensions of living with respiratory support, including individual strategies for managing respiratory insufficiency so as to maximize the benefits of technology and minimize its social and psychological costs.

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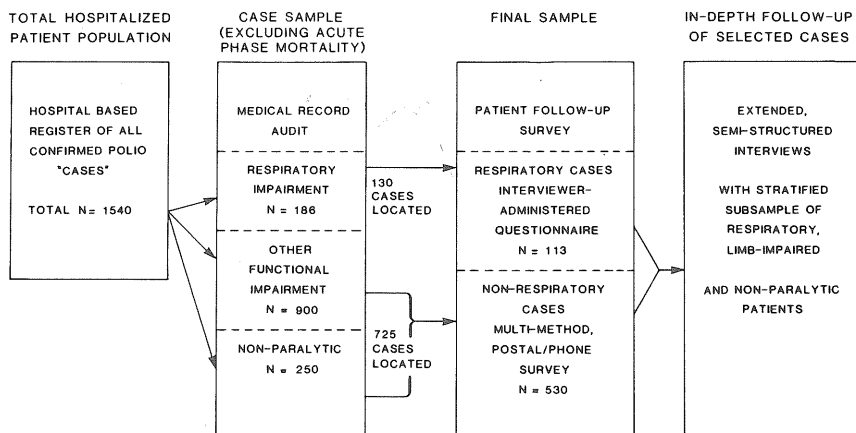
COMBINING EPIDEMIOLOGICAL AND QUALITATIVE METHODS

In our previous paper dealing with epidemiological issues in the analysis of post-polio aging effects [2], we suggested that research in this area had been limited by restriction to people who had remained in contact with the system of rehabilitation medicine. These have tended to be the more severely impaired patients [2]. In designing the Manitoba follow-up surveys, we were able to draw a representative sample of post-polio patients by going back to a register of 1,540 cases admitted to a centralized treatment facility between 1952 and 1959. In the respiratory follow-up study, 113 of 130 surviving individuals were interviewed (Fig. 1). The epidemiological survey was unable to explore in depth the impact of polio on the lives of individuals, particularly those with respiratory polio. The in-depth interviews were an attempt to document these lives and to explore with those concerned their own more personal interpretations of the meaning of disability and technological change [3]. The combination of an epidemiological approach to case finding and sample selection with in-depth qualitative analysis of life histories offers the advantages of what are frequently depicted as alternate approaches to the analysis of disability and illness behavior.

Data collected in the 2 surveys allowed us to document the occurrence—or nonoccurrence—of key events in people's life histories, such as marriage, divorce, changes in residence, occupational and educational careers, and medical events such as surgery or hospital admissions. This information allowed us to document some of the long-term consequences of a polio-related disability. For example, both severity of respiratory impairment and family support system were highly correlated with the probability of permanent

FIGURE 1

SAMPLING DESIGN FOR MANITOBA POLIO FOLLOW-UP SURVEYS



hospital residence for those who were young adults at the time of the epidemics.

The second function of the life history interviews was to provide a mechanism for placing the descriptions of the individual disability experience within the context of the broad social and political changes influencing individual adaptation. These changes include developments in medical and rehabilitation technology, public policy, and programs for the disabled, as well as public attitudes toward individuals with disability. This paper primarily documents the impact of changing respiratory-support technology upon individual adaptation—particularly adaptation to late, polio-related aging effects.

ASSESSING PSYCHOSOCIAL ADAPTATIONS THROUGH IN-DEPTH INTERVIEWS

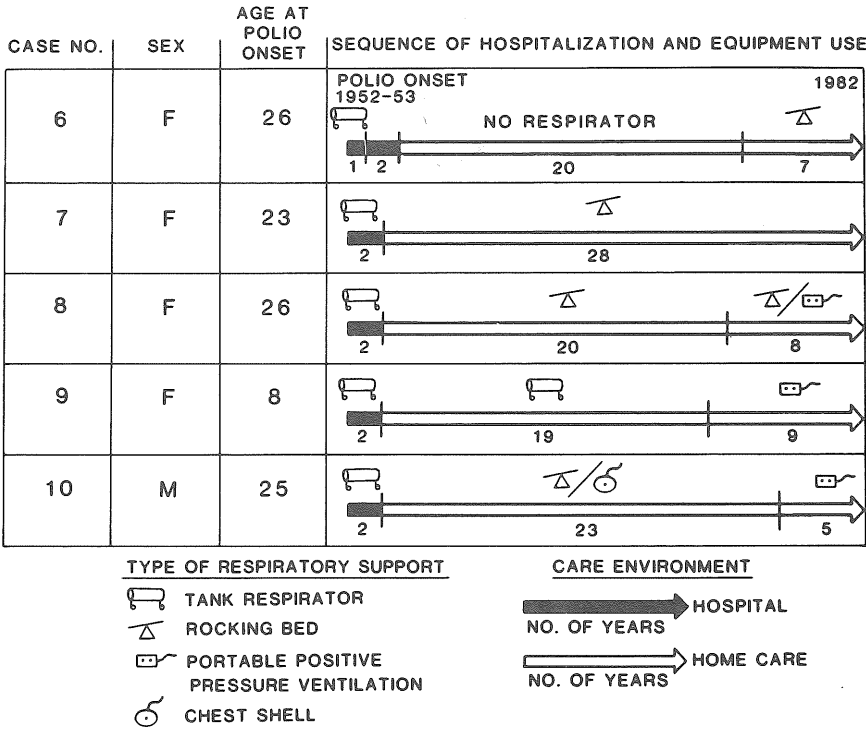
The psychosocial impact of changing respiratory support technology on those with residual respiratory impairment was documented through in-depth interviews with 10 selected respirator-dependent individuals. All had experienced a significant decline in function following the postacute phase and had been forced to rely on a variety of methods of mechanical support for 12 or more hours a day. They were selected from among a group of similarly disabled people because of their range of experience with support equipment and accessibilities. Their life histories should be regarded as a series of case studies of individuals whose personal history has been shaped, in part, by technological change.

There were 10 respondents, 5 women and 5 men. All had major limb disability in addition to respiratory impairment. The majority had been in their mid-to-late 20s at onset of polio and, at the time of the interviews, their ages ranged from 39 to 66 years. Each person was interviewed on 2 or more occasions using a semistructured schedule. These formal interviews were tape recorded and transcribed in full and supplemented by interviews with other people with a polio-related disability and with clinicians who were involved in acute and continuing care. Table 1 summarizes the history of respiratory support equipment use among 5 of the respondents who spent extended periods as inpatients during the past 3 decades. The Table shows the changing patterns of life support and, in 3 cases, sequences of community care interspersed with hospitalization. Table 2 shows the same histories for the 5 individuals who were able to live predominantly in home care settings.

Changing Respiratory Support Technology and Patient Careers

All people who had polio have been able to benefit from advances in general medical knowledge applicable to their needs. However, for profoundly

TABLE 2.
HISTORY OF RESPIRATOR DEPENDENCE
AMONG HOME CARE RECIPIENTS



tages, allowing welcome modifications in a previously restricted life-style, but requiring the development of a repertoire of coping mechanisms to manage their idiosyncrasies.

Patient Careers: Functional and Psychosocial

The changes in the life experience of people with post-polio disability over the period since onset can be viewed as a series of conceptually distinct though empirically overlapping biophysical, functional, and psychosocial careers. These careers encompass changes in biological processes, their influence on the performance of the activities of daily living, and the impact of both on the quality of life and life chances [5].

Epidemiological studies of the career of a disabling condition focus upon changes in functional status using measures of mobility, performance of activities of daily living or, in the case of respiratory impairment, the number of hours of daily dependence on mechanical ventilators.

We will mention only briefly the epidemiological results from the total

cohort of surviving respiratory patients for comparative purposes, because these results were more fully described in the proceedings of the First Research Symposium on the Late Effects of Poliomyelitis [2]. In assessing changes in functional status, a combination of survey data and medical record audit provided measures at 3 points in time: at onset, after rehabilitation, and in 1980. For the respiratory survey respondents, as a group, there was a significant improvement in levels of mobility ($P < .001$) and performance of activities of daily living ($P < .001$), but only a marginally significant improvement in people's level of dependence upon respiratory support equipment ($P = .09$). Multivariate analysis was used to examine late aging effects. A stepwise multiple regression revealed significant negative correlation ($P = .02$) between changes in respiratory status and age. This suggests that older patients in the most disabled group showed less improvement in their level of respiratory function or had experienced a greater recent decline in their capacity than had younger patients.

LIFE HISTORICAL APPROACHES TO DISABILITY CAREERS

Unfortunately, this kind of epidemiological analysis tells us very little about the details of the changes in day-to-day respiratory function and even less about the range of individual experience with late-onset respiratory insufficiency. To illustrate historical analysis, we will discuss the life events and changing patterns of use of respiratory technology in one case. Figure 2A illustrates the use of a time line summarizing the number of hours the patient depended upon the support of a respirator each day. Many of the changes in respiratory function and relationships with respiratory support equipment were influenced by dramatic changes in health status or family events. These life events are shown across the top of the graphs (Figs. 2A–2C) in 3 segments of a time line illustrating adaptations in the 3 decades of the person's experience since the onset of polio. Adaptation to respiratory support was also influenced by developments in the technology of life support and policy changes influencing the availability of services. These contextual factors are noted along the bottom of the time line.

The onset of acute respiratory effects of paralytic polio was experienced by the patient when she was 8 years old as she joined the patients treated in iron lungs during the 1953 epidemic. Initial respiratory management of the patient's condition was influenced by the designation of a centralized treatment center and provision of sufficient respirators to care for the 186 respirator-dependent individuals surveyed. The Figure shows the person's experience with "weaning" or gradual reduction of machine dependency. It also illustrates her experience in combining use of the iron lung with the rocking bed and chest shell respirator. The portion of the time line denoting

FIGURE 2A
CASE EXAMPLE OF PATIENT CAREER SHOWING LIFE EVENTS AND LEVEL
OF DEPENDENCE UPON RESPIRATORY SUPPORT EQUIPMENT

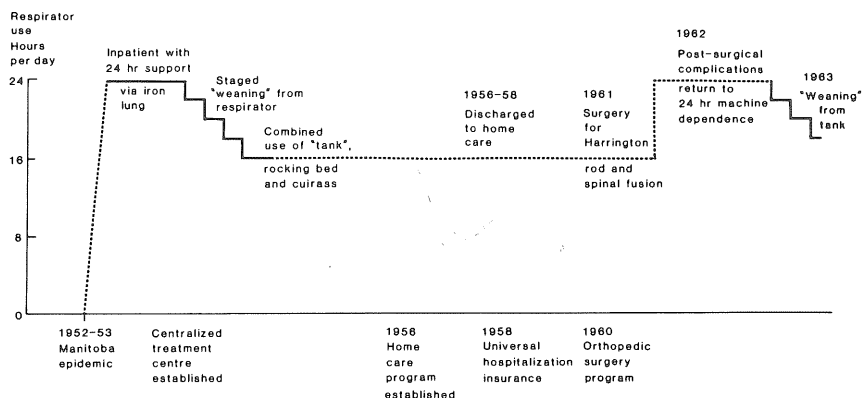


FIGURE 2B
CASE EXAMPLE (cont.)

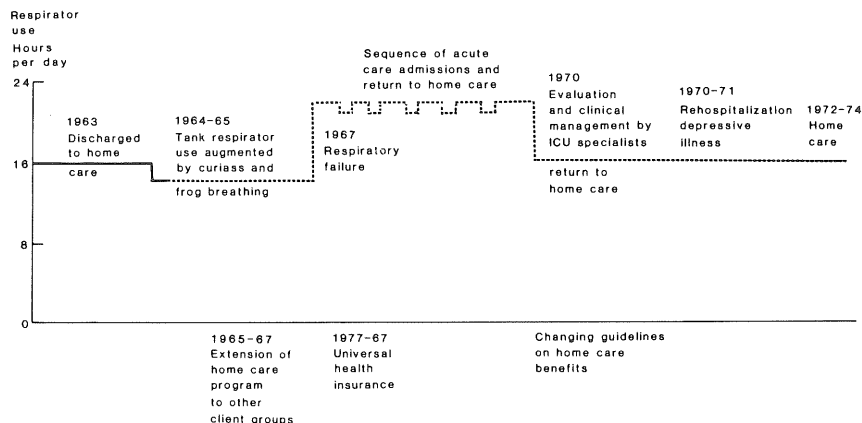
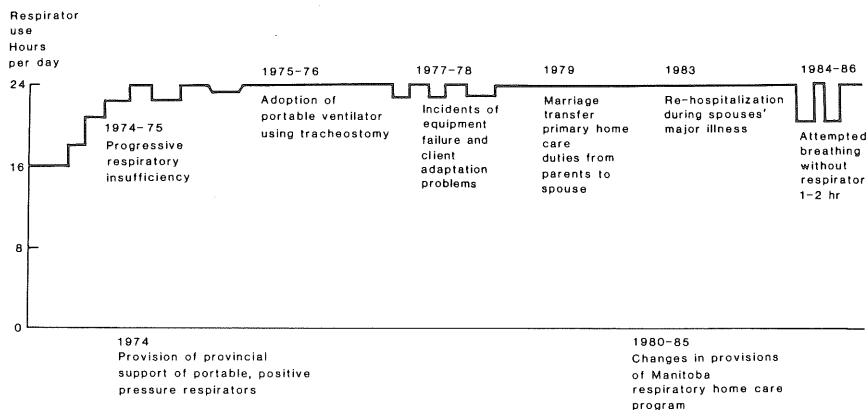


FIGURE 2C
CASE EXAMPLE (cont.)



context emphasizes the impact of development of the first provincially supported respiratory home care program. The patient was discharged to home care after trial home visits. A second event that influenced management was the availability of universal, government-sponsored hospital insurance supporting both inpatient services and support of home respiratory care equipment. At the end of the first decade, the patient experienced an unanticipated period of respiratory insufficiency as a result of complications of orthopedic surgery, a series of major surgical procedures including Harrington rod placement and spinal fusion. Figure 2B shows the second decade of the person's post-acute experience, including a second sequence of weaning and experimentation with alternate support systems. In 1967, the patient was again readmitted to hospital after respiratory insufficiency and again returned to 24-hour dependence upon the tank respirator. During the early 1970s, the overall management of the patient's respiratory care was taken over by a group of intensive care specialists with particular expertise in newer forms of ventilation technology. The patient was hospitalized with a series of other problems, including depressive illness.

The third decade of postrehabilitation life experience (Fig. 2C) is perhaps most relevant to our immediate interest in late aging effects of poliomyelitis, although it is difficult to limit as specific time horizons identified for the onset of late effects. In the middle 70s, the patient began to experience a sequential loss of respiratory function and was readmitted to hospital with respiratory insufficiency. In 1975, she was provided with a wheelchair-mounted, positive-pressure ventilator and tracheostomized. A year later, she returned to home care. During the early experience with portable positive-pressure equipment, the patient reported a number of incidents of equipment failure and described her problems in adapting her activity patterns to the use of the equipment. In the same time period, she married and the primary personal care functions transferred from her parent to her spouse. During the 1980s, the patient was hospitalized during the time her spouse was hospitalized with a myocardial infarction. The final segment of the patient's experience involved a program of supervised independent breathing, which the patient used to try to develop more active ability to breathe on her own for short periods of time.

The total sequence of this individual's career illustrates the range of variations in people's adaptation to technology that must be considered in evaluating the experience of late aging among respirator-dependent people. The point is that research must take into consideration the range of technological interventions and impact of other medical events and external forces, such as changes in the availability of medical programs, to properly understand the total sequence of the patient's respiratory experience.

THE PSYCHOSOCIAL IMPACT OF RESPIRATORY SUPPORT TECHNOLOGY

One reason for focusing on the total career of the respirator-dependent person, rather than only upon the more recent experience of late aging effects, was that current use of technology was influenced by previously established patterns of psychosocial adaptation. It therefore seems appropriate to mention the development of people's "ideologies" about disability and their coping strategies.

In common with all others who developed respiratory paralysis, the 10 people interviewed for this study were placed in an iron lung during the acute phase of the disease. The time they spent confined to the lung varied from 3 to 18 months. Following recovery from the acute phase, all entered a period of respiratory rehabilitation during which they were encouraged to begin to breathe independently. This transfer from passive breathing in the iron lung to respiratory independence was referred to as "weaning." The aim was to help the patient develop maximum ability with the muscle function that remained; the method used was simply to remove the person from the tank. All respondents described this period as an ordeal. As one man recalled:

"The sister came around about ten every morning like a sergeant major and said 'Everybody breathe' and the orderlies or the nurses would open up our iron lungs and you'd gasp. I'd just turn blue, it was really grim."

This process of recovering respiratory and other physical functions was facilitated by a dominant feature of the patient's institutional context. This was a prevailing ideology that stressed independence and minimal resort to mechanical support. Currently referred to as the rehabilitation model, this approach saw recovery and reentry into the community as a function of willpower and individual effort [6]. In the early stages of rehabilitation and disability career, the majority subscribed wholeheartedly to this ideology, minimizing wherever possible dependence upon help and technology. This stress on independent effort was well expressed by one of the female respondents whose respiratory and functional capacities had declined substantially over the years:

"We were encouraged to keep pushing ourselves to the limits. You just kept going, whatever you were doing you just kept on doing it until you were so tired you couldn't go any further. And we sort of had this drilled into our heads."

This orientation toward setting goals and persevering until they were realized became problematic during the mid-to-late 60s when a decline in respiratory capacity (or other aging effects) began to affect the quality of their lives.

ONSET OF RESPIRATORY DECLINE AND ADOPTION OF TECHNOLOGY

Our interviews suggested that the career of respirator-dependent people with polio-related disability can be characterized in terms of 3 stages: independent respiration, partial dependence on respiratory technology, and total dependence on mechanical support. Following rehabilitation in the immediate postacute phase, 8 of the respondents became largely independent of respiratory support. Of the remaining 2, one continued to use an iron lung and chest respirator, and the other a rocking bed. All enjoyed a period of stability lasting several years before experiencing a decline in respiratory status. This decline took one of 2 forms. In some cases, onset was slow and insidious and often went unrecognized for long periods of time, while in others, a crisis, sometimes precipitated by respiratory infection and sometimes not, indicated respiratory insufficiency and led to the readoption of mechanical support. In both instances, the diagnosis of inadequate ventilation heralded a new period of adaptation in which the respondents were forced to adjust anew to the constraints of respiratory technology.

Those respondents who experienced insidious onset complained of a number of symptoms. Prominent among them were tiredness, lack of energy, and repeatedly falling asleep during the day, even in midconversation. At that time, neither patients nor physicians appear to have anticipated a decline in respiratory function and a diagnosis of carbon dioxide retention was sometimes a long time in coming. Given the lack of physical signs and the prevailing ideology of striving for independence, some people initially interpreted their problem as motivational rather than physical. Some of the respondents reported an initial reluctance to return to mechanical support, with one woman refusing to use her rocking bed until she discovered what a difference it made to her well-being.

For those who initially achieved independence from mechanical ventilation, the decline in respiratory status was a 2-stage process. The first stage consisted of a partial return to mechanical support. Here, rocking beds and other forms of technology were used during part of the day or at night. Many respondents reported that during this stage, they gradually increased their use of respiratory equipment, almost without realizing it, in an attempt to maintain their oxygen supply, energy levels, and quality of life. Subsequently, increasing respiratory impairment led to a search for newer and more effective technologies. For all, the solution was found in the positive-pressure ventilators previously described. The 6 most seriously impaired exchanged the older methods of support for permanent connection via a tracheostomy, while the remainder used a ventilator with a mouth tube to supplement the methods they had always employed.

Those respondents with tracheostomies can be considered to have progressed to the second stage in the process of respiratory decline: mechanical ventilation for 24 hours a day. This resort to total respiratory dependence, referred to by one respondent as "the end of the road," coincided with the final rejection of the rehabilitation ethic that had been the guiding principle of the respondents' lives during the early years of disability. One respondent described a fellow patient who continued to resist respiratory support:

"There's one patient I feel should be on a machine and isn't. He still has the feeling that the harder you work, the better you're going to be. You have to get all that out of your head and go back and approach it from another angle."

The respondents' statements reflected an acceptance of dependence upon technology if it maintained levels of functioning and enhanced the quality of life. In some cases, this new attitude represented the culmination of a gradual realization that the struggle to remain independent might do more harm than good. Several respondents indicated that they had become more critical of the early approach to rehabilitation emphasizing individual effort. Several people discussed contemporary explanations of the post-polio syndrome stressing the effect of premature exhaustion of muscles that had remained functional. As one woman said, "It only stands to reason, if you work something for so long it's going to quit working." Subsequently, new technology and new attitudes to technology have combined to produce significant and sometimes dramatic changes in these people's careers.

The people we interviewed in depth fell into 2 distinct groups. The first we called "partial users"; they used mechanical support more than 12 hr/day, usually a combination of a rocking bed and positive-pressure machine with mouth tube. The others we called "total users": permanently connected to the positive-pressure machine by tracheal airway, they did not breathe independently at any time during the day. These groups were distinct in terms of problems they encountered in everyday life and the extent and nature of psychosocial adaptation to technology.

Those respondents who did not have a tracheostomy, most of whom were able to breathe independently for up to 12 hours, supplemented their own breathing by using a rocking bed and a positive-pressure machine with a mouth tube. The latter, activated by a sucking action, allows the individual to take air when he or she wishes. These people would sleep on a rocking bed and also had to set aside time during the day when they could use the bed, the positive-pressure machine, or both. All were forced to stick to a strict daily routine to ensure that their needs for oxygen were met. Most had been advised to use the positive-pressure machine for 5 min/hr, but found that too disruptive of daily living. Many had developed their own routines more compatible with the time and activity pattern of their everyday lives.

Adaptive Strategies

These daily routines were modified or extended in order to cope with extraordinary circumstances, usually social visits or other activities that might keep them away from home for a few hours. Then they would need to prepare for the activity by spending additional time on the bed, the machine, or both. The following day's routine would also need to be modified with additional time allocated to respiratory support. This was necessary to cope with the tiredness that always followed an unusually long period of independent breathing. In this way, social activities had to be planned and paid for in terms of additional time given to mechanical ventilation. Permanent connection to a ventilator by a tracheostomy freed the individual from these daily routines and the constraints they involved. At the very least, continuous ventilation by a portable machine meant that the person was never forced to stay at home.

Despite the use of respiratory support equipment for 12 or more hours a day, these people found that their oxygen supply and energy levels remained problematic. Adaptation to limited energy supplies required the use of coping strategies designed to maximize the benefits to be gained during the course of everyday life. Three were evident: 1) selective allocation—using limited reserves of energy to accomplish valued activities and abandoning others; 2) pacing—estimating energy levels and matching to levels of activity; and 3) short cutting—finding methods of minimizing energy expenditure in performing activities of daily living.

Those using positive-pressure machines with a tracheal airway encountered a different set of problems. They had to adapt to the idiosyncrasies of the machines they used, find ways of maximizing the benefits derived from them, and develop a repertoire of coping skills in order to manage the problems these technologies involved.

All those respondents who had made the final transition to a ventilator with a tracheal airway readily agreed that it had had a positive impact on their lives. The main benefit was an increased supply of energy. They not only achieved more during the course of the day, but felt like achieving more. Breathing was easier, there was no need to allocate time or effort on maintaining an air supply, talking was easier, they reported less fatigue, a better appetite, fewer episodes of respiratory infection, and fewer problems with the urinary tract previously caused by long hours spent lying down. Most positive-pressure equipment users reported improvements in their overall psychosocial adaptation and attitude towards living. One of the women, formerly confined for hours in an iron lung, said, "I can sit up; I see more of life." During the 7 years she had used the ventilator, she had found a job and, having persuaded a national airline to carry her with her equipment, had made several trips around the North American continent.

Despite these advantages, most respondents described a counterbalanc-

ing set of negative effects associated with the adoption of new equipment. Problems encountered by those using positive-pressure ventilators with tracheal airway include: 1) coming to terms with tracheostomy and the visual stigma of the tracheal airway; 2) developing skills of breathing and talking with the machine; 3) locating a primary care giver who is willing to accept the broad and complex caring role associated with equipment usage and maintenance; and 4) coming to terms with loss of independence in respiration and its consequences.

This loss had minimal impact where the individuals felt they were still able to manage for some time should the machine break down; these people remained confident that they would survive until the problem could be solved. The others experienced a loss of self-esteem, feelings of vulnerability, and an even greater dependence upon trained personnel. As one of these respondents said, "What's going to happen if I get a problem? How would I breathe on my own? I've got to have someone there all the time; I need constant attention."

The crisis feared by these respondents did have a foundation in fact. Many had experienced instances of machine failure that involved physical discomfort, anxiety, or life-threatening situations. Consequently, they had to be constantly vigilant to reduce the chances of machine failure or recognize and head off a potential crisis. One of the respondents described this process of problem recognition and maintenance necessary to avoid crisis situations arising from machine failure:

"You have to get to know what it feels like when the valve is not working or if there is a leak in the hose somewhere and you have to get to know the feel of it when the pressure drops too low and take action."

This extra care and attention in terms of routine case and crisis management meant that "total users" had no choice but to tolerate additional intrusion by others in their daily lives.

CONCLUSION

Despite the current view of technology as a liberating force, the cases presented here suggest that the situation is much more complex. For those with post-polio respiratory disability, the impact of respiratory support technology on biophysical processes is fairly clear cut. Mechanical methods of ventilation restore or enhance respiratory capacity, improve energy levels, and ensure survival both in the short and the long term. The social impact of such technology and its role in coping with a chronic disabling condition may, however, be more ambiguous since it necessarily involves a compromise between freedoms and constraints [7]. While the benefits conveyed by positive-pressure ventilators are substantial, they were only realized at a cost. Improvements in energy level, mobility, and well-being have to be balanced

against the imposition of new routines, new management strategies, and new concerns. In most cases, these benefits and costs were balanced by the individual and produced significant and dramatic changes in the conduct and pattern of everyday life. For many of the people described here, technology both solved problems and generated new dilemmas for themselves and their support networks.

Our examination of costs and benefits of respiratory support equipment has attempted to provide a qualitative understanding of the interaction between biophysical changes in late aging effects and changing technology. Cross-sectional epidemiological and clinical research focusing upon aging effects may risk decontextualizing the experience of people who have utilized medical care and rehabilitation services during the past 3 decades. Respirator-dependent people's experience of late effects cannot be isolated from the sequence of changes in the technological and organizational structure of medical care, rehabilitation, and life support. The impact of individual and family life events and personal adaptive strategies in evaluating the outcome of technologically sophisticated life-support systems must also be considered. By combining a qualitative understanding of life history with epidemiological and clinical follow-up, we ultimately may be able to respond more adequately to the individual priorities of people who depend upon long-term respiratory support.

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DISCUSSION

DR. KOHL: In dedication to you I will read a quote that a patient gave to me because I think it epitomizes your talk. "And what is as important as knowledge?" asks the mind. "Caring and seeing with the heart," answered the soul.

DR. ANTEL: Dr. Kohl and Dr. Halstead, of the people who walk in the door at your institute, how many of them do you think really took advantage of all that you were offering?

DR. HALSTEAD: The number of people whom I think were helped is going to be hard to assess. Some people did come and just wanted to have validation that they were having a new problem. That was probably the largest group, and just to walk in the door and be accepted and have someone say I understand what you are going through and not be discounted, to have their symptoms validated, was very powerful medicine. I don't have percents on this, but there were a number of folks who had to come several times to hear that message, who, as Dr. Smith has mentioned, desperately needed a brace. We all know that on the first visit, it is the last thing they want to hear, and so we learned over a period of time not to talk about bracing or about a motorized cart or wheelchair. What we do is establish a rapport and trust with the patient. We demonstrate that we can, in fact, make their lives more comfortable with a very simple device like a lumbar roll, or whatever, to help their posture. When they realized that we knew what we were doing, then we might say a short leg brace would really make your posture better, make you walk more comfortably, and make you less fatigued.

DR. KAUFERT: Also, I think in response to your question about the resource you can have programs like the one that started in Manitoba, where we had a group of older clinicians that had a baseline register that allowed us to do good follow-up research. Not until very recently has a generation of young clinicians been willing to take that register or the case finding and baseline research that was done at Houston or is now being done at Mayo with a clinical follow-up. I think that there is a real dilemma of meeting both of those programs. We established some pretty good data on Central Canadian cases, but we didn't have a group of clinically oriented researchers or a clinical facility that could provide the follow-up. We raised the question by doing a survey, but the ethical question is, do you also not need to move to the clinical program? One of the resource issues is, do you have a generation of clinicians with the interest that are willing to take up that challenge as happened in Houston.

The Environmental Aspects of the Post-Polio Syndrome

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The environmental aspects of health and disease are becoming much more clearly defined. The adverse influences of environmental incitants on wounded target organs often have been seen by people working in environmental medicine. Because of these observations, a preliminary survey of environmental influences was done on post-polio patients who exhibited the post-polio syndrome.

MATERIALS AND METHODS

Subjects

Seventeen post-polio patients who had developed "post-polio syndrome" (mean = 49 years, ages 31 to 63; 5 men and 12 women) were evaluated initially (Table 1). Polio history, with symptom and sign scores, was obtained from each patient. All patients but 2 could walk with either crutches, braces, or post-polio orthopedic prostheses, while the remaining 2 were confined to wheelchairs. All 17 patients had experienced lower limb weakness as their chief complaint. In addition, 2 had upper limb weakness. Nine patients also complained of pain as disabling as the weakness. All patients were evaluated for the effects of pollutants upon their signs and symptoms to search for triggering agents. The effects of these pollutants and environmental antigens were studied using a controlled environmental unit and program as a scientific basis for the study. Testing of most patients was performed in an environmentally controlled outpatient area using cutaneous, oral, and inhaled challenges of incitants in air, food, and water. Two patients were studied in the inpatient area. Signs and symptom scores were calculated periodically, and this was followed through at home with further observations. The patients were followed over a year after initial challenge to further define and confirm

TABLE 1. Symptoms in Post-Polio Patients Before and After Treatment

Patient	Symptoms
Before treatment	
17	lower limb weakness
(2)	upper limb weakness
(9)	pain—muscle and bone
After one year of treatment	
14	gone
1	recurrent
2	no change

triggering agents and degrees of improvement. All had given informed consent and were not charged for their evaluation or vaccine treatment.

The Controlled Environment

The scientific basis for our studies is in the development of the controlled, "less polluted" environment for testing and treating. This controlled environment is in an isolated wing of the hospital designed specifically to be less polluted. All construction was done to minimize outgassing of fumes and particulates. Usually porcelain, steel, and ceramic tile are used for the walls and floors. No smoking, perfumes, or synthetics are allowed in the wing. All bedding materials are of natural fibers. Incandescent lights are used. The air is filtered by a series of specially designed depollution devices [1]. Nontoxic cleaning substances are generally used. Air analysis is monitored by particulate counts, gas chromatography, and mass spectrometry to assure continuous depollution. Less contaminated drinking water is made available by charcoal filtration, distillation, or use of natural spring water in glass containers. Food is raised, transported, stored, and prepared in the relative absence of petrochemicals, aluminum, copper, gas, and synthetics.

Food, mold, pollen, dust and dust mite antigens for challenge are specifically prepared using only NaHCO_3 and NaCl as extracting agents and then frozen [2]. Chemical challenge incitants are made in a similar manner [3]. Intradermal skin challenges were done using 1 to 5 serial dilution. Inhaled challenges were done in a controlled booth within the controlled environment. Doses of chemicals used for the inhaled challenge were phenol $<.0024$ ppm, formaldehyde $<.20$ ppm, petroleum ethanol $<.50$ ppm, chlorine $<.33$ ppm, and pesticide 2, 4, DNP $<.0134$ ppm (Table 2).

Each subject carried out dietary and life-style modifications, including avoidance of harmful foods and ingested or inhaled chemicals (phenols, petroleum alcohol, insecticides, chlorine). Injection therapy of inhalants, foods, and some chemicals were performed for all but one patient. Often home environments were modified to eliminate smoke, mold, gas heat, routine

TABLE 2. Triggering Agents Defined by Inhaled, Oral, and Intradermal Challenge Under Environmentally Controlled Conditions

Patients	Incitants
15	inhalants (pred. molds)
17	chemicals
16	formaldehyde
14	cigarette smoke
12	polio vaccine
9	terpenes
8	perfume
8	petroleum ethanol
7	chlorine
5	diesel
4	phenol
4	newsprint
17	foods (sensitive to 7 or more, eg, coffee, tea, cane sugar, wheat, corn, milk, beef, chicken, eggs)

pesticides, and other synthetics. This was done to decrease total body ambient pollutant load.

RESULTS

Of the 17 subjects, 14 developed marked improvement of their weakness, and 8 became pain free. One patient improved intermittently for weeks, then lapsed back to his old symptoms for 2- to 3-week periods. Two patients showed no improvement. Fifteen were sensitive to inhalants, predominantly molds. All 17 patients were food sensitive and 15 of these were sensitive to 7 or more foods. All 17 patients tested for chemicals had multiple triggering agents; all 17 were sensitive to formaldehyde, 14 to cigarette smoke, and 10 to pesticides. Eight were sensitive to petroleum alcohol and reacted to phenol. Twelve had a positive skin test to polio vaccines. The other 5 refused testing of the vaccine. Two patients got dramatic relief from pain and weakness with .05 cc of 1/25 dilution of the polio vaccine on numerous occasions. The other 3 who allowed treatment with the diluted vaccine noted no relief. Seven patients were extremely sensitive to chlorine and had to give up their swimming pool therapy because they realized that the adverse effects that occurred after such therapy were the very ones they were trying to eliminate. Two patients had inhaled double-blind challenges in the hospital unit with reproducible results (Table 3). These correlated well with the skin provocation. There were a minimum of 34 associated symptoms and signs in these 17 patients (Table 4). These included ear, nose, and throat (ENT) signs of headaches, dizziness, and recurrent rhinosinusitis in 9; gastrointestinal upset in 4; overweight; edema;

TABLE 3. Ambient Dose-Inhaled Toxic Chemical Challenge—Double Blind

Booth	Dose PPM		Pulse Change		Flow Meter Change		Symptom Change		EKG		Reproducible TX3	
	Pt. 1	Pt. 2	Pt. 1	Pt. 2	Pt. 1	Pt. 2	Pt. 1	Pt. 2	Pt. 1	Pt. 2	Pt. 1	Pt. 2
Placebo #1 (spring water)	5 cc	5 cc	0	0	0	0	0	0	0	0	+	+
Placebo #2 (filtered water)	5 cc	5 cc	0	0	0	0	0	0	0	0	+	+
Placebo #3 (filtered water)	5 cc	5 cc	0	0	0	0	0	0	0	0	+	+
Petroleum ethanol	<.5	<.5	0	3 SD	0	0	0	+	0	0	+	+
Formaldehyde	<.2	<.2	3 SD	2 SD	3 SD	0	+	+	0	+	+	+
Phenol	<.5	<.5	0	2 SD	0	0	0	+	+	0	+	+
Chlorine	<.33	<.33	0	2 SD	0	0	0	+	+	0	+	+
Pesticide (2,4DNP)	<.0134	<.0134	2 SD	2 SD	0	0	+	+	0	0	+	+

Done in hospital environmental wing, under strictly controlled environmental conditions, after de-adaptation for at least 4 days.

WF = white female; WM = white male; SX = symptom(s).

Weakness, asthma: Pt. #1, 55, WF, SX—asthma, weakness; Pt. #2, 45, WM, SX—arrhythmia, weakness, pain.

TABLE 4. Accessory Symptoms Reproduced by Challenge Under Environmentally Controlled Conditions and Alleviated by Long-Term Treatment

Ear, nose, throat	
headache, dizziness, recurrent rhinosinusitis	9
Gastrointestinal upset	
bloating, abdominal cramps	4
Weight gain (nonedematous)	3
Edema	10
Respiratory difficulties	
severe asthma	1
breathless	4
short of breath	3
Hypertension	2

and respiratory difficulties, including one very severe case of asthma; and many other symptoms. These were brought under control with environmental manipulation in 14 of the 17 patients. Long-term follow-up of the 14 improved patients showed general return of well-being and renewed vigor. Two patients who had not been able to work returned to their jobs. Several others who had feared loss of jobs because of decreasing function were able to perform better.

DISCUSSION

In 1970, Dickey [4] reported a case of a post-polio patient who clearly had been made worse by exposure to environmental pollutants and improved by avoidance. Mandell (personal communication) further built upon this observation in presenting a paper on several post-polio patients who had environmental triggers, and Bailey [5] reported on oral antigen therapy at the first International Research Symposium on Polio in 1984 suggesting environmental triggering. Our work using the Environmental Control Unit as a scientific basis for studies of chronic diseases suggested that perhaps some of the late polio problems might be due to an overload of environmental pollutants on wounded target organs [6-11]. It has been shown previously that many chronically recurring inflammations and postinflammatory diseases were significantly influenced by definition and elimination of environmental pollutants. Techniques are well developed for the precise definition of triggering agents using particle counters, gas chromatography and mass spectroscopy in controlled environments [12]. Studies of patients evaluated under environmentally controlled conditions can also be carried out correlating improvement with serial analysis of blood organic chemicals and pesticides [13, 14]. Challenge tests verifying deterioration of the clinical condition also can be performed [15]. These principles and techniques were used with the post-polio patients in this series with successful demonstration of triggering

agents in all the cases that might suggest an adverse environmental aspect. Several subtle ancillary signs such as rhinosinusitis were elicited in the post-polio syndrome patients.

Many signs and symptoms elicited were cyclic, subtle, and periorbital, including digital and pedal edema, and suggested increased vascular disturbance. Often cold sensitivity, petechiae, purpura, spontaneous bruising, and adult acne were seen. Heightened odor sensitivity to perfumes, pesticides, and newsprint, was observed in many patients. The vascular dysfunction and the odor sensitivity seemed to be clues to the presence of environmental influences in the post-polio syndrome patient. The rapidity with which an incitant could bring on the symptoms of the post-polio syndrome after de-adaptation was impressive. We frequently observed individuals who were doing well revert suddenly and completely to the post-polio syndrome with symptoms of weakness or pain within a few minutes after a small exposure. Symptoms would then clear up in a day or two and the patients returned completely to their base line state. This observation apparently tended to reinforce the initial testing with provocation of symptoms.

Following up these post-polio patients for a minimum of one year allowed us to see that their improvement was in fact real, and they were able to live a much more vigorous and pain-free life. It further confirmed that our initial impressions that the challenge tests were valid. All successful patients not only received inhalant, food, and chemical injections, but also changed their life-style and living environments. Some interesting observations were reported by these patients and correlated well with observations of environmentally sensitive non-polio patients. The most glaring was that the chlorine and other chemical odors emanating from the patients' therapeutic swimming pools often reproduced their symptoms of pain, aching, and weakness. Exposure to gas or other fossil fuel heat would often render them nonfunctional. Not only did certain foods trigger these patients' syndrome, but often also chemical odors in the work environment.

At least half of the patients credited the program to saving their jobs. Two other patients actually became employable when they had not been previously. One patient who had been confined to a wheelchair was again able to walk with crutches. Mechanisms of environmental triggering were not part of this study. However, the post-polio syndrome patient does not appear to differ from other environmentally influenced patients. So far, dysfunction appears to be the result of inappropriate vascular regulation via the involuntary nervous system. Analysis of a few post-polio environmentally sensitive patients suggests involvement of certain enzyme detoxification systems such as superoxide dismutase, glutathione peroxidase, lipid peroxidase, aryl hydrocarbon hydrolase, and chromium P-450 systems, as well as changes in the suppressor and helper T-lymphocytes. The concept of reducing environmental

pollutants in post-polio patients with wounded target organs is clearly scientifically sound. Though results in this preliminary study were encouraging, further study should be carried out when funding is available. It should be pointed out that probably not all post-polio syndrome patients are as environmentally influenced to the degree that the patients in this study were; 15 patients who initially wanted to enter the study dropped out after initial contact before any testing could be done. They may have felt that defining the environmental aspects of their symptoms did not apply to them. Only the testing of a larger number of patients can answer this question.

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DISCUSSION

DR. BRADLEY: To be sure of those experimental effects, one presumably needs to have reproducibility and double-blind controls for that application

and to demonstrate that you get the same on each occasion. Did you have those controls?

DR. REA: That is why I presented the environmental care program in which we have had thousands of double-blind studies with reproducibility. With the post-polio patients, we had some blind challenges, but we did not have double-blind studies because of the situation. These subjects were outpatients in a less controlled area. This whole study was very expensive because we supplied all the vaccines and everything with no charge to the subjects; we just did not have the funds to put them in the hospital under the double-blind condition. Two patients did have inpatient double-blind challenges that were reproducible.

DR. KAUFERT: In addition to the design issues of looking for controls, I think there is an additional dilemma that has to do with labeling of the way symptom-specific questions are asked in a group that is already defined as post-polio. It is like the written questionnaire given to a group that are already defined as survivors v a nonspecific symptom questionnaire given as a general health instrument. It seems to me that it isn't surprising that the symptom manifestations were talked about in post-polio terms, even physically measurable in those terms. If you had been dealing with a multiple sclerosis (MS) population and done an environmental challenge, their symptomatology in a trial in which they were labeled as MS might as well have been expressed in terms of that kind of symptomatology. So, I think there is another design issue that is also very relevant.

DR. REA: I would agree, and that is another reason for using the individual as his own control. If you can get him in basal state without signs or symptoms and then rechallenge him, you are showing effect.

DR. SPENCER: The implication of your paper is that the environmental pollutants that are of concern are principally those agents that spew from the smoke stack. And yet I wonder whether or not one is possibly missing a critical area for concern and for increased attention, namely, the possibility there may be agents present naturally within foodstuffs that are of potential importance. We do know, for example, that there are molten uran toxins in certain unusual foodstuffs such as the chickling pea. We know that casaba, which feeds some 500 million people in the world, can, under certain circumstances, cause ataxic neuropathies. Recently, an unusual amino acid has been identified that is able to produce a primate motor system disease and is a possible cause of ALS on Guam. So here are just three examples where individuals in developing countries have been exposed to natural chemicals in food, who subsequently have developed molten uran conditions. Now, we assume in the United States that our food is, of course, free of such natural compounds. But, in fact, no one has ever looked.

DR. REA: Well, some people have looked and that was the point of testing food alone, because you are exactly right. We know of alphatoxin in some foods. That is known to be a toxic poison. We also know, according to data, that there are thyrogenic compounds in millet that can increase thyroid problems. According to some of Gardner's studies, there are plants that are very similar to the phenylated compounds that we have talked about that may cause problems. So you are entirely right, and I think that we cannot assume anymore that the water is safe, that the food is safe, and that the air is safe. I think that there are environmental aspects to living and that these can influence our disease processes and our health processes. If we can define and eliminate those or manipulate them in our favor, we are much better off. It doesn't say that it is always going to cure the problem, but some people will respond and some people won't.

DR. MUNSAT: I would like to join the chorus of those who urge very strict controls before claiming therapeutic efficacy in any sense. I think those of us who see a lot of post-polio patients are fully aware of the very significant psychosocial stresses that those patients are under. Some of this has been discussed, and most probably this group of patients are likely to be very high placebo responders, but this data has not been presented.

The Post-Viral Syndrome and Polio Study: Long-Term Effects of Viral Disease

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INTRODUCTION

One hundred patients with post-viral syndrome, characterized by prolonged malaise, debility, extreme fatigue, muscle pain, and headache, were studied. In each case, a history was obtained that at the onset of their problems, a viral infection had occurred in one of 4 ways.

The first was an epidemic form, often in an institutional community, as in myalgic encephalomyelitis outbreaks. In our study, we included some patients who had had the Royal Free Disease, in which a group of staff at the Royal Free Hospital, London, suffered an acute viral illness with the sequelae described. This included a staff group from the Royal Preston Hospital, people from its environs, and an additional group from an epidemic in Essex, England. The second manifestation was as infectious mononucleosis at the outset. The third form was a flu-like illness with upper respiratory tract infection, while in a fourth group, symptoms began after an infectious gastrointestinal episode.

The other study group consisted of 10 patients who had a history of poliomyelitis; they complained of increasing weakness, fatigue, and headache. Of the 100 patients with post-viral syndrome, 25% had suspected Coxsackie infections, 42% had infectious mononucleosis with positive Paul Bunnell test, and 33% had gastrointestinal or upper respiratory tract infections.

All patients presenting with the post-viral syndrome of malaise, debility, extreme fatigue, headache, and muscle pain also reported polysymptomatic complaints on a medical questionnaire. Their polysymptomatic complaints particularly involved the gastrointestinal tract: nausea; diarrhea; constipation in bouts; abdominal discomfort, especially after meals; bloating, which is almost pathognomonic of food sensitivity; and mucous colitis. The diagnosis of irritable bowel syndrome is commonly applied to people with these com-

plaints. In addition, eczema, urticaria, and itching skin were common, as were rhinitis and sinusitis with episodes of postnasal drip, sneezing and coughing, and recurrent upper respiratory tract infections, including bronchitis and bouts of asthma. Frequency of micturition was often reported and on occasion, periorbital edema or dependent edema of the feet and hands occurred. Sleep disorders were also predominant, as were depression, irritability, mood swings, and difficulty in concentration. Another major feature was recurrent glandular enlargement.

One of the main problems in the group of patients studied was restriction of their activities of daily living; they were unable to perform work adequately, and household duties were limited because of fatigue, headache, and muscle pain. Some of the characteristics of the headaches described were classic migrainous episodes with teichopsia, nausea, vomiting, and unilateral headaches. Occasionally, common migraine was described in which the headache was all encompassing and accompanied by nausea and vomiting. Sometimes the headache was nuchal.

Further questions on the questionnaire related to common foods eaten, inhalant sensitivities, and chemical sensitivities. Table 1 shows the most common symptoms.

The 10 post-polio patients complained of debility with neurologic sequelae of wasting of muscle groups, weakness that had previously been extant, sporadic extreme weakness, and polysymptomatic other complaints, as in the other post-viral groups. These problems all began 26 to 35 years after the original viral disease.

METHODS

Patients were admitted to our unit and the following program was adopted:

- 1) fasting for the first 4 days,
- 2) food challenges for the second 4 days,
- 3) neutralization of foods for the rest of the days,
- 4) inhalant and chemical testing during the first 4 days, if the patients were well enough,
- 5) rare food regimen for patients unable to fast,

TABLE 1. Most Common Symptoms

Lethargy	100%
Depression, anxiety, mental confusion	100%
Nausea, bloating after meals	87%
Muscle and joint aches	66%
Sore throat	54%
Eating for comfort	54%

- 6) nutritional assessment and counseling—rotation diet, vitamin and mineral supplements,
- 7) ecologic counseling—chemical clear-out, and
- 8) instructions on immunotherapy.

Standard investigations undertaken included pathology and biochemistry profile, T-lymphocyte subsets, immune complexes, full examination with microscopy and culture of urine, mineral analysis of blood, sweat, and hair, and other investigations as necessary.

The food challenge tests were conducted in the following manner. An average portion of the food to be challenged was given to the patient. The resting pulse and other existing symptoms were noted. Pulse and symptoms were monitored at 20, 40, and 60 minutes. Other observations were monitored as appropriate, such as blood sugar, electrocardiogram, and peak flow readings. Patients found to be food sensitive by elimination and challenge were given vaccines as ascertained by the provocation/neutralization technique.

Chemically sensitive patients were those who had a history of constant reactions to diesel, petrochemical fumes, perfume, tobacco, cleaning agents, industrial chemicals, work-place chemicals, newsprint, gas for cooking, or exposure to dressings on clothing, such as in fabric stores. The patients were treated with vaccines for foods, chemicals, and inhalants and then assessed at periods of one month, 3 months, 6 months, and one year during the ensuing year.

RESULTS

Response to the patients' activities was the major means of assessment. The results are tabulated in Table 2.

This study indicated that the patients with the post-viral syndrome have abnormal T-lymphocyte indices. Furthermore, the majority have food, chemical, and inhalant sensitivities and respond to treatment with vaccines and good environmental control. As the group of patients with post-polio syndrome responded in a manner similar to those with a post-viral syndrome, the assumption is that the post-polio syndrome could well be due to food, chemical, and inhalant sensitivities.

TABLE 2. Results of Treatment

Grading		Response
0	Did not continue with treatment	8%
1	No change in general condition	20%
2	Improvement in general condition	12%
3	Able to return to work or lead normal social life	60%

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DISCUSSION

DR. JUBELT: I want to make a comment first, then I want to ask a few questions. I think it is well known that at the same time there may be multiple enteroviruses active in the community, there may be other enteroviruses besides Coxsackie that are causing the syndrome. Obviously, in addition, there can be other viruses, and at times, some of these patients may not even have a viral infection. I have 2 questions for you. One, I didn't hear you comment about how long these symptoms persisted after the viral infection and two, please comment on treatment, as my impression is that these post-viral patients generally get better on their own, over a period of time.

DR. MONRO: The outbreaks of the epidemic viral infections had occurred some time before we actually saw the patients. So, we had to go according to the history of what had been established in those individuals. The outbreaks were in the early 60s, including the Royal Free disease, and in 1978. We have been seeing patients over the last 3 years, and their post-viral syndromes have actually been extant in many of these patients intermittently since their original illness and had actually become much more severe before they presented to us. We were not able to do any of the antibody viral titers for the patients. We had to rely on the documentations that had been done before. But, in the Royal Free outbreak, it was an entire community of people who had actually suffered the same acute illness during the period of 6 months and gave the name of the "Royal Free Disease" to this particular complaint. We can't actually say that with these people who had the epidemic disease, that they all have the same problem, though in some of them, Coxsackie had actually been demonstrated to be a causative agent. You asked what length of time the virus diseases continued. In the ones who had had infectious mononucleosis, the length of time varied between 10 years and 2 years. In general, we did not see them until the actual complaint had been persistent for about 2 years. They had all been told that it will go with rest and so on, but, in fact, it was perpetuated, and in many of them it was also fluctuant. They would have a period of remission for a few weeks and then they would be unable to work again.

DR. KAUFERT: Following on with that point about the variability over time, both you and the previous speaker have used the concept of using people as

their own control and you have measured them in a couple of points and time. But, you have used general symptom check lists. The GHQ or the Cornell Medical Index, any of those on a normal population will yield between a 45% and 65% "yes" rate for some general kinds of symptoms like the ones that you have given; and when they are given to normal populations longitudinally, you will find variability of 15% to 20% in symptom reporting over a one-year period. Therefore it is very difficult using the kind of design that implies an individual is his own control to really attribute that to anything but the individual variability over that year that you have measured them.

DR. MONRO: The problem is that we are dealing with people with polysymptomatic complaints and our major assessment was in fact the activities of daily living. That is why we used a score of whether or not people were able to perform their ordinary activities. In fact, the majority of the people who had come to us had been unable to undertake a normal day's work, whether it be housework or work out of the home. But, 60% of our people actually were able to be restored to full-time work for a considerable period toward the end of their treatment.

DR. JOHNSON: It sounds to me like you were describing a depressed person to us. In your protocol, is there any evaluation of the psyche?

DR. MONRO: No, we didn't have a psychologic evaluation with our particular group of people. I think that when you are trying to treat a group of people, because this is a treatment program rather than particularly designed with all the research data in mind, we found for certain, that by treating them we were able to reverse their conditions in the majority of patients. I think that shows that, at least the treatment was effective even if it was helping their psyche as well.

Quantitative Electromyography After Poliomyelitis

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INTRODUCTION

In patients who have had polio, progressive late muscular weakness (progressive post-polio muscular atrophy—PPMA) occurs in muscles that were not weak originally, as well as in muscles that were clinically involved. From muscle biopsy and electromyography (EMG) findings, as well as histologic studies of the spinal cord in patients and animals with polio, we know that acute poliomyelitis produces widespread motor neuron damage, even when a patient's history suggests only restricted involvement. Thus, it is undoubtedly true that late progression occurs in muscles that have previously undergone partial denervation and reinnervation. Two hypotheses for the physiologic abnormality of PPMA are: 1) there is progressive loss of motor units (MUs) due to the normal aging process, which may be accelerated in anterior horn cells (AHCs) that have been damaged previously by polio virus; or 2) there is progressive dropout of parts of the reinnervated MUs (peripheral fractionation) from loss of nerve terminal axons or branches. If either of these hypotheses is true, the most severely involved muscles should show the greatest progression, and the degree of deterioration might be proportional to the size of the reinnervated MU. Progression occurring in areas that were not themselves severely involved would implicate a diffuse, systemic process, such as a metabolic abnormality or latent virus. To determine how to distinguish among these possibilities, this paper will address the following questions:

- 1) What is the EMG pattern in patients who have had polio in the past? How does this differ from other diseases of the anterior horn cell (AHC)?
- 2) Can EMG patterns determine whether the muscles with progressive weakness are those that were most severely involved initially?
- 3) How can EMG help distinguish between the progressive loss of MUs and peripheral fractionation of the MU?

EMG TECHNIQUES

Surface electrode recordings of the compound muscle action potential (CMAP) evoked by maximal stimulation of the motor nerve can be used as a measure of muscle atrophy. The area under the negative peak of the CMAP is the best measure of the total number of innervated fibers in the muscle that responds to a single nerve stimulus.

Repetitive stimulation of the motor nerve at low frequencies ($<10/\text{sec}$) will produce a reduction in the size of the CMAP elicited by consecutive stimuli if a significant number of muscle fibers fail to respond because of defective transmission in the peripheral nerve or neuromuscular junction. This technique is of limited sensitivity in detecting abnormal neuromuscular transmission, however, which is best detected by single-fiber EMG measurement of neuromuscular jitter (see below).

Conventional EMG recordings made with concentric needle electrodes (CN-EMG) measure the electrical activity predominantly from muscle fibers that are within only a few millimeters of the active electrode surface. Typically, motor unit action potentials (MUAPs) thus recorded are large, complex, and reduced in number in disease of the motor neuron or peripheral motor axon. Instability of MUAPs is usually seen during the process of reinnervation, indicating abnormal neuromuscular or neuronal transmission. In analyzing the interference pattern (IP) recorded with a concentric needle electrode, the amplitude and number of spikes ("turns") in the signal are measured to obtain information about the size of MUAPs and recruitment of MUs, even those activated only at high force levels, which cannot be assessed by other EMG techniques. In anterior horn cell disease, the IP contains turns of increased amplitude and decreased number per unit time.

Single-fiber EMG (SF-EMG) uses a small, selective recording surface on a concentric needle electrode to record the action potentials from individual muscle fibers. This permits measurement of the fiber density (FD), which reflects focal grouping of muscle fibers, a sensitive indicator of collateral sprouting. Increased FD may be seen 3 to 4 weeks after nerve injury (Fig. 1), before changes of reinnervation can be seen on muscle biopsy or conventional EMG studies. Thus, increased FD may be the earliest and most subtle evidence of reinnervation [1]. In SF-EMG recordings, abnormal neuromuscular transmission is seen as increased variability of the intervals between action potentials from muscle fibers in the same MU, the neuromuscular "jitter." When neuromuscular transmission intermittently fails at individual motor endplates, impulse blocking is seen on SF-EMG. Neuromuscular jitter may be increased early in nerve disease while denervation is occurring, before collateral sprouting causes increased FD (Fig. 1). Jitter may be marked during the process of reinnervation, probably because the newly formed synapses are immature and not capable of supporting normal neuromuscular transmission (Fig. 1). As reinnervation becomes established, the jitter

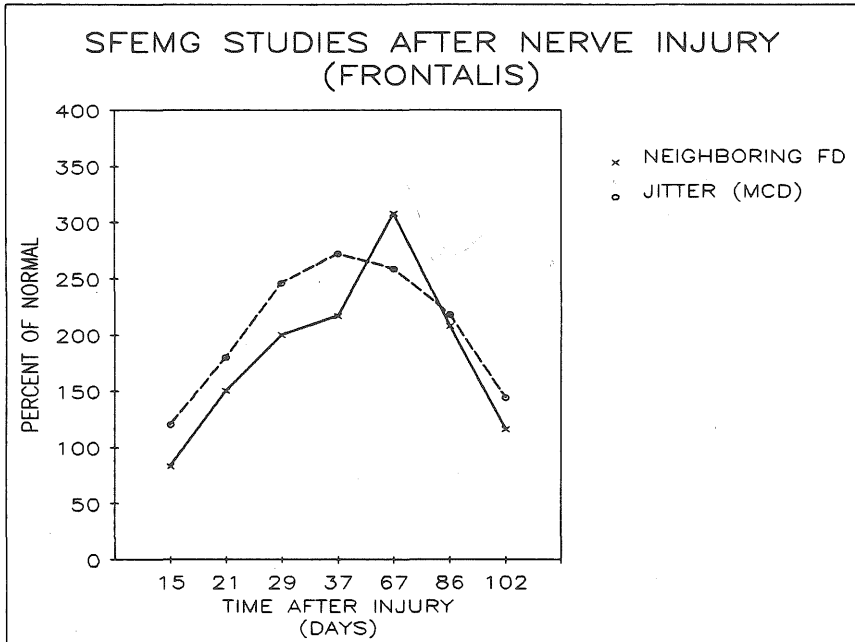


Fig. 1. The results from serial SF-EMG studies in the frontalis muscle of a patient following surgical trauma to the facial nerve. Jitter was increased in 20% of potential pairs at the time of the first study, 15 days postoperatively. Jitter and fiber density were most markedly abnormal 7 to 10 weeks after the injury; both measurements fell dramatically thereafter, indicating that the reinnervated motor units underwent remodelling, probably as axons regrew from the site of the injury. Abbreviations: SF-EMG—single fiber EMG, FD—fiber density, MCD—mean difference of consecutive interpotential intervals. (Neighboring fiber density = $FD - 1$)

decreases (Fig. 1) [2]. This implies that neuromuscular transmission improves as the synapses mature.

Neurogenic blocking [3] is recognized in SF-EMG recordings when 2 or more action potentials from the same MU block simultaneously (Fig. 2). These blocking potentials are usually late components in a complex MUAP. Jitter may be up to 500 μ sec between these action potentials and earlier components. To exclude the possibility that the blocking action potentials may originate from split muscle fibers that share a single endplate, jitter should be greater than 5 μ sec between them. Typically, the neurogenic blocking in a motor unit increases with the activation rate and responds little, if at all, to the administration of edrophonium.

Macro EMG was developed to record MUAPs that reflect the electrical activity from all muscle fibers in the MU [4, 5]. Fiber density is measured with the same electrode to assess the arrangement of muscle fibers within the

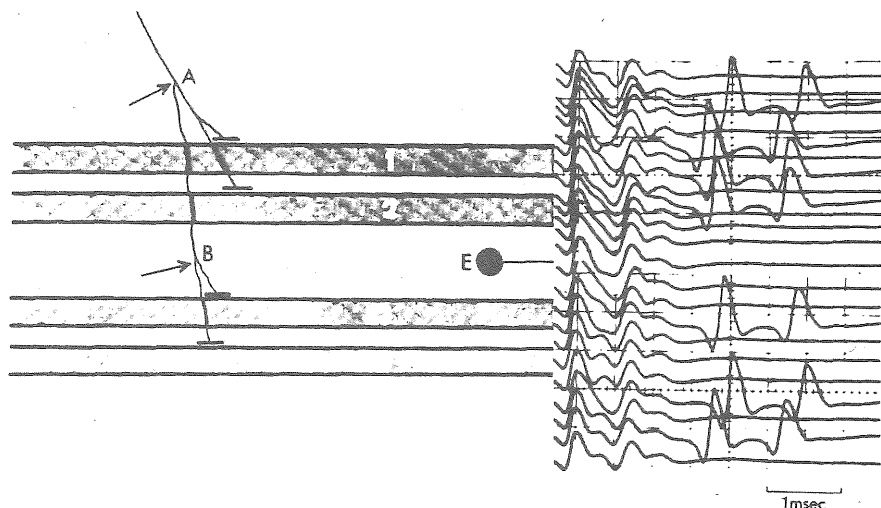


Fig. 2. Neurogenic jitter and blocking. Schematic drawing of SF-EMG recordings from 4 muscle fibers innervated by the same nerve axon, 2 of them (3 and 4) from a sprout branching off at A. Recordings at the right from electrode E show intermittent concomitant blocking of the last 2 potentials, which also behave as a unit with large jitter in relation to the earlier components of the MUAP. (From Stalberg E, Thiele B: Transmission block in terminal nerve twigs. A single fibre electromyographic finding in man. *J Neurol Neurosurg Psychiatry* 35:52-59, 1972, with permission.)

MU. Computer simulations predict that the amplitude and area of macro MUAPs increase with the number and size of muscle fibers in the MU [6]. In normal muscle, the shape of the macro MUAP differs among different muscles. Peaks in the macro MUAP correspond to portions of the MU innervated by nerve branches. The amplitude of macro MUAPs increases with age. The amplitude and area of the macro MUAP typically increase in reinnervation, and the size of the macro MUAP is an indication of the reinnervation capacity of the MU.

EMG PATTERNS IN ANTERIOR HORN CELL DISEASE

In all diseases of the peripheral nerve or anterior horn cell, atrophy may be seen as reduced size of the CMAP elicited by maximal nerve stimulation.

Decrementing responses to repetitive low frequency nerve stimulation have been described in 67% of patients with amyotrophic lateral sclerosis (ALS), more frequently in atrophic muscles with more frequent fasciculations [7].

Spontaneous electrical activity characteristic of denervation (fibrillations and positive sharp waves) is seen in all AHC diseases.

In ALS, EMG abnormalities are usually found diffusely in all muscles, even in the earliest recognizable stages of disease when the clinical manifestations may be limited to one limb or a few muscles. Increased jitter may be the earliest EMG abnormality seen in some muscles, suggesting that neuromuscular transmission is abnormal during the degenerating stage of the disease. In most individual muscles, FD and the size of MUAPs recorded with CN and macro EMG electrodes are increased to similar degrees, indicating that reinnervation is relatively homogeneous throughout the MU territory. In muscles in which strength is normal, however, FD may be increased in the absence of increased CN or macro EMG MUAP size.

FD and MUAP size increase before there is significant weakness in the tested muscle, indicating that loss of motor units is adequately compensated by reinnervation in the early stages of disease (Figs. 3 and 4). The highest values of FD and MUAP size are seen in muscles with moderately severe

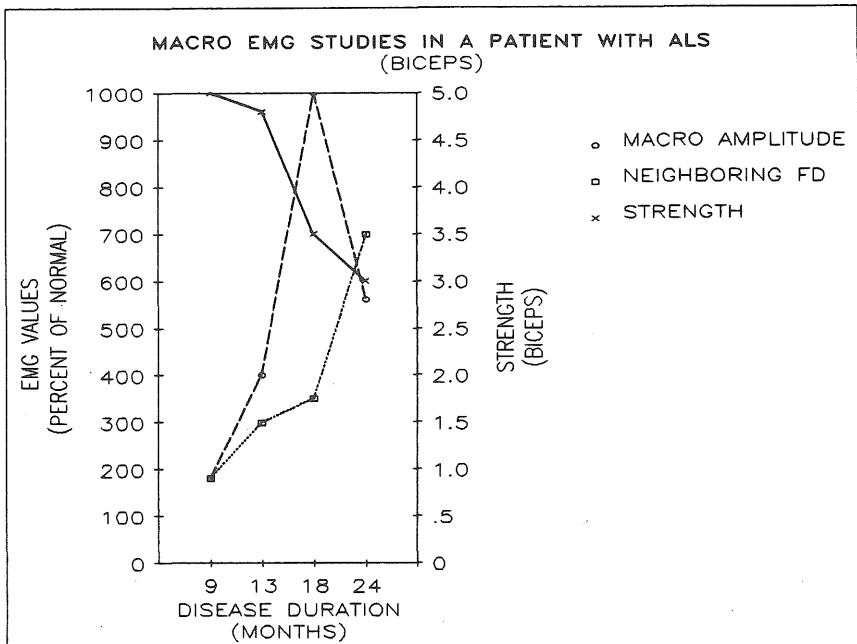


Fig. 3. Serial macro EMG studies from the biceps muscle of a patient with ALS. Macro-MUAPs and FD were increased at the time of the initial study, when the strength in the tested muscle was normal. Macro-MUAP size was greatest 18 months after the first symptoms were noted. The macro-MUAP size fell thereafter, suggesting that the reinnervated MUAPs were undergoing peripheral fractionation. Abbreviations: ALS—amyotrophic lateral sclerosis, FD—fiber density. (Neighboring fiber density = FD - 1. Strength was graded by the MRC scale.)

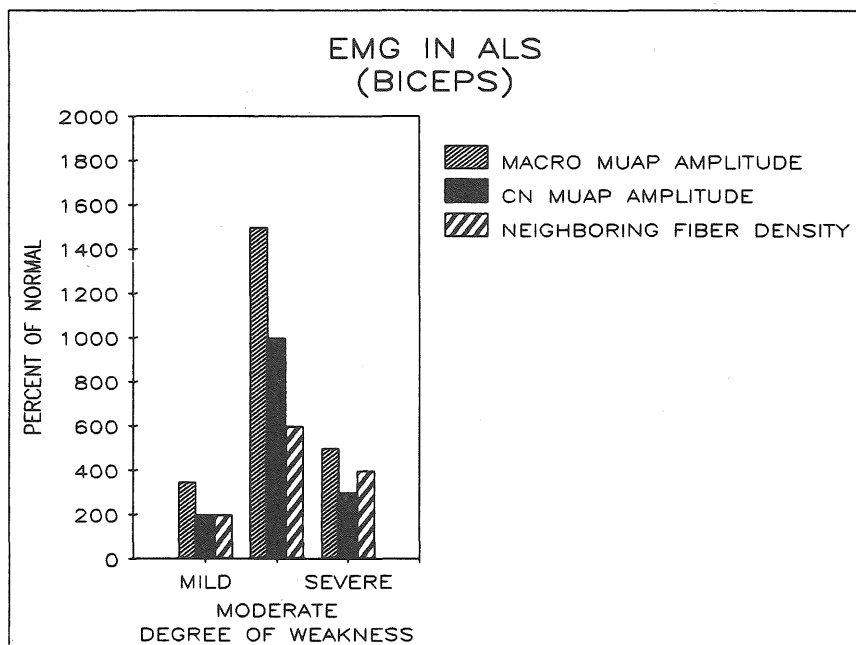


Fig. 4. A comparison of normalized values of mean macro and concentric needle (CN) EMG motor unit action potential (MUAP) amplitude with fiber density in the biceps muscles of patients with ALS. All 3 measurements are increased in patients with normal strength or mild weakness and are most markedly elevated when the weakness is moderate, indicating that this is the stage of disease when reinnervation is maximum. All 3 measurements fall as the weakness becomes severe, suggesting that the motor units are undergoing peripheral fractionation.

weakness (Fig. 4). This implies that in this stage of disease, the maximum reinnervation capacity of the MUs has been reached but is not sufficient to compensate for the progressive loss of MUs. FD and MUAP size are not as great in muscles that have severe weakness, indicating that peripheral fractionation of the MUs has occurred in these muscles as the disease progressed (Figs. 3 and 4). The greatest amount of jitter and blocking is seen when the disease is most rapidly progressive. The highest values of FD and MUAP size are seen in chronic, slowly progressive motor neuron disease, such as spinal muscular atrophy (Fig. 5).

In the patients with ALS whom we have studied, macro MUAP amplitude was increased up to 20 times normal in the biceps and up to 5 times normal in the tibialis anterior. This demonstrates a pronounced capacity for reinnervation.

In all types of AHC disease, IP analysis demonstrates increased ampli-

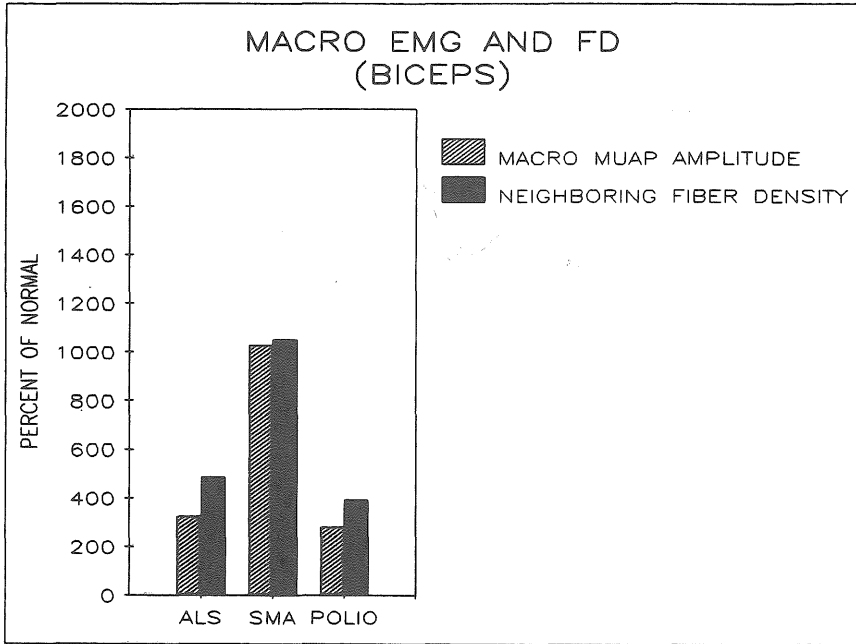


Fig. 5. Macro EMG motor unit action potential (MUAP) amplitude and fiber density measurements in patients with ALS, spinal muscular atrophy (SMA) and past polio. Normalized mean values are shown for measurements made of 574 MUAPs in the biceps muscle of 35 patients with ALS, 32 MUAPs from 3 patients with SMA, and 174 MUAPs from 10 patients who had had polio. (Neighboring fiber density = FD - 1)

tude of the turns in the IP and a decrease in the number of turns per unit time. More detailed information about EMG patterns in AHC disease is available elsewhere [8, 10-15].

In syringomyelia, there is increased FD and occasional increased jitter, with marked variability among different muscles [8]. The greatest jitter is seen in muscles with the most marked recent progression [9].

In normal subjects, FD increases with age, especially after age 70 [16]. These changes, more marked in some muscles than others, are especially prominent in distal muscles. In men whose occupation involves chronic muscle use, these changes are more marked, suggesting that age and chronic use produce mild nerve terminal denervation and reinnervation [17].

EMG FINDINGS AFTER POLIOMYELITIS

In patients who have had polio in the past, as in other neurogenic diseases, muscle atrophy can be demonstrated as low amplitude CMAP

responses to nerve stimulation, whether or not there has been progression of weakness. In these patients, neurogenic abnormalities are found in most muscles by conventional EMG [18, 19], and IP analysis [20, 21]. Spontaneous activity, consisting of fasciculations or fibrillations and positive sharp waves, are also seen in many muscles in these patients years after the acute denervating process, whether or not there has been clinical evidence of progression [18, 19].

Following acute poliomyelitis, FD is increased in most muscles and does not seem to be correlated to the age of the patient or the length of time since the acute infection [19]. Jitter is also increased in many muscles [19, 21], and greater jitter has been reported in the muscles of patients with PPMA than in those of post-polio patients without progression [21]. The amount of jitter and blocking is greatest in MUs with the highest FD and, in patients without progressive weakness in one study, this was correlated with the age of the patient and the time since acute polio [19]. These observations suggest that MUs achieve stable reinnervation after acute poliomyelitis and later undergo deterioration, perhaps as part of the normal aging process.

Neurogenic blocking has not been seen in patients with old polio [19, 21], even in those with PPMA [21, 22]. This observation has been taken as evidence that PPMA does not involve loss of MUs or groups of muscle fibers, which would be expected to produce neurogenic blocking. However, drawing firm conclusions from the absence of neurogenic blocking in PPMA would require knowing the frequency with which it is seen in other diseases by the laboratory performing the EMG. If PPMA resulted from loss of single muscle fibers from reinnervated MUs, neurogenic blocking of single axons might be seen as blocking in single muscle fibers that increased with firing rate. This pattern would not be distinguishable from that of abnormal neuromuscular transmission unless it was demonstrated that there was little response to edrophonium at the individual endplate.

We have examined a small number of patients who have had polio and have found increased FD and macro EMG MUAP size similar to that seen in ALS (Fig. 5). Because of the small sample size, we cannot make any comparisons between the findings in muscles with stable strength and those with progressive weakness.

None of these EMG techniques, singly or in combination, applied at one point in time, distinguish among different types of AHC disease. Serial measurements performed in progressive AHC disease, such as ALS, demonstrate progressive changes that reflect initial denervation, followed by reinnervation and progressive loss and fractionation of MUs (Fig. 3). Similar serial studies in post-polio patients may demonstrate whether or not there is progressive degeneration of AHCs in this condition. Let us now address the questions we raised initially.

- 1) What is the EMG pattern in patients who have had polio in the past?

How does this differ from other diseases of the AHC? We have found no difference to date in the EMG findings in individual muscles between patients who have had polio, with or without progressive weakness, and patients with ALS. All patients have varying degrees of reduction in CMAP size, spontaneous activity, neurogenic CN and macro MUAPs, increased FD, and increased jitter in some muscles. We cannot yet comment on the significance of differences in the distribution and severity of various findings among muscles.

2) Can EMG patterns determine whether the muscles with progressive weakness are those that were most severely involved initially? This is the subject of a current study, results of which are pending. We would expect that CMAP size, IP analysis, FD, macro EMG MUAP size, and jitter measurements would be more abnormal in the muscles that had been more severely involved by the initial polio. It has yet to be determined whether these are the muscles that are more likely to become progressively weaker later.

3) How can EMG help distinguish between progressive loss of MUs and peripheral fractionation of the MU? Studies performed at one point in time cannot answer this question in patients who have had poliomyelitis in the past, since all the EMG abnormalities seen after polio could be residua of the acute disease. If there is progressive loss of MUs, as long as the reinnervating capacity of the MU isn't exceeded, there should be a progressive increase in the size and decrease in the number of turns in the IP. Macro MUAP size and FD should increase. CMAP size would probably not change in a slowly progressing process as long as reinnervation was keeping pace with denervation. If there is any type of progressive peripheral fractionation without adequate reinnervation, CMAP size, the amplitude of turns in the IP, and macro MUAP size should all progressively decrease. If branches of the peripheral axon are lost, with subsequent reinnervation, there would be no change in CMAP size but some increase in all other EMG parameters; the changes in these measurements would be less marked than if individual muscle fibers were progressively lost from the MUs followed by reinnervation. If individual muscle fibers are lost from the MUs *without* subsequent reinnervation, fiber density, as well as CMAP and macro EMG MUAP size and IP turns amplitude, should fall.

These considerations form the basis for serial quantitative EMG studies that we are currently performing in patients who have had poliomyelitis to see how muscles with progressive weakness differ from those with stable strength.

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DISCUSSION

DR. McCOMAS: You showed that in ALS, near the end of the course, there is a reduction in size of the macro EMG recordings. If, in fact, what is happening

in the post-polio patients is a loss of fibers from an anterior horn cell that cannot maintain them all, we should see the same reduction in size in the macro-EMG recording; and, my question is: Have you made any comparisons of macro-EMG in muscles that are progressing with those in muscles that are not progressing equally severely in individual patients?

DR. SANDERS: That is one of the major questions that we want to answer and is the subject of a study that is currently in progress.

DR. GOW: As a non-neurophysiologist, can you tell me whether you get any EMG changes according to the functional metabolic state? For example, if there are changes in nutrition before or after exercise, can you get changes in EMG?

DR. SANDERS: One should not see significant changes in the electrical activity that we are recording under most conditions of normal metabolism. One thing that has to be borne in mind, however, is that all of these EMG measurements are based on a sample of a population of motor units, and it is not impossible that under conditions of fatigue or other metabolic stress, the population of motor units that is active might change. That might show up in our studies as a change in the size of motor unit action potentials. That is something that we have not really looked into in great detail, but it is something that we must consider.

DR. DALAKAS: Did you see any differences between post-polio and ALS in the degree of fiber density? From the histologic point of view, there is grouping, and the grouping in post-polio appears to be much larger than in ALS.

DR. SANDERS: In looking at the fiber density, again, we have to bear in mind the effect of sampling. We use certain measures to give us an overall number for fiber density. We must also consider the distribution of muscle fibers within individual MUs throughout a muscle. As yet, we do not have enough data to make a comparison that would allow us to say whether there is a significant difference in either of these 2 factors between patients who have polio and patients who have ALS. Since ALS is not a static process, if we measure the fiber density in any muscle of a patient with this disease, we are going to find differences compared with the other side depending upon the severity of the involvement of the 2 muscles. One of the characteristics of ALS, especially early on in the disease, is that there are significant differences in the distribution of abnormality among different muscles, depending upon the stage of the disease in each muscle.

DR. BERGER: Just a comment on the distribution of changes. We have found that although the patients are able to identify very accurately which muscles are apparently getting weak, we found that in many of these patients, the electrophysiologic changes of jitter, blocking, and some spontaneous activity

far exceeded the limitations of their muscle. They may complain only of one limb being involved, but the homologous muscles on the other side, in which there were no complaints at all, were also showing evidence of motor unit disintegration.

DR. SANDERS: Yes, I think that is one thing that has come out of these and other studies that previously have been performed. We can see all these EMG abnormalities in any muscle, but they don't seem to be restricted to the muscles in which there is clinical evidence of progressive weakness. Our approach is to do serial studies in muscles that we define as potentially becoming progressively weaker and comparing them with studies performed in the opposite side to see if there are differences.

Three Novel Electrophysiologic Tests for Patients with Muscle Weakness*

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INTRODUCTION

The purpose of this chapter is to describe 3 electrophysiologic tests of muscle function that are applicable to patients with muscle weakness of indeterminate origin. These tests differ from those employed in routine EMG laboratories in that they are relatively novel; there are, however, indications that they may eventually become accepted in electrophysiologic laboratories [1]. Of these tests, we have applied only one, motor unit counting, to patients with previous poliomyelitis and on single occasions only. Our intention, however, is to embark on a more comprehensive research program on the post-polio syndrome (PPS) in which all 3 tests will be used in a prospective manner. Such a program is intended not only to identify the site of muscle weakness, but to determine the time course of any deterioration. Each type of examination will now be described, together with illustrative results.

TEST 1—MOTOR UNIT COUNTING

The ability to obtain a gross estimate of the number of functioning motor units in a muscle was recognized in 1967 and, after many trials and modifications, the first published reports appeared in 1970 with a more complete description in the following year [2, 3]. The essence of the method is to stimulate a muscle indirectly in such a way that a comparison can be made between the mean amplitude of the motor unit potentials and the whole muscle response (maximum M-wave). Examples of the technique are shown in Figure 1 for the extensor digitorum brevis muscles of a normal subject and of a 43-year-old man who was complaining of increasing muscle weakness 33

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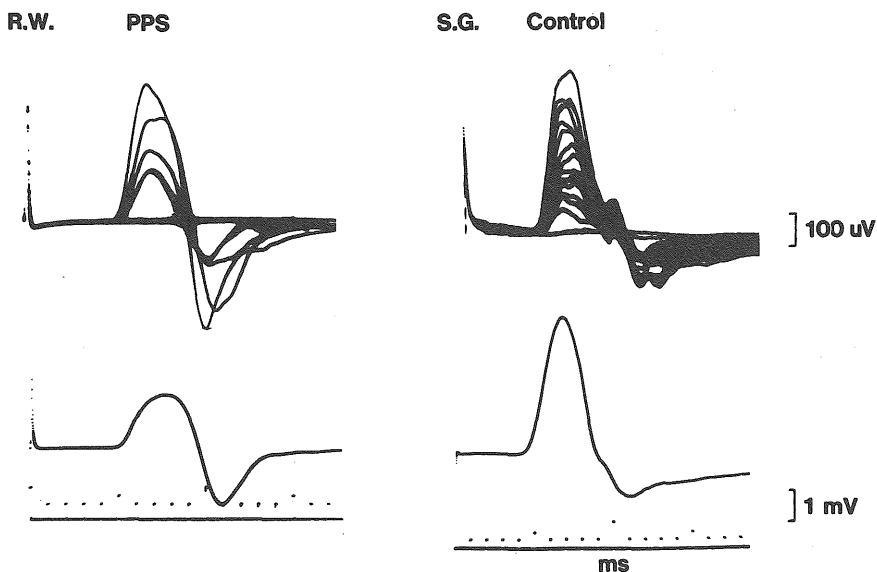


Fig. 1. Motor unit counts in extensor digitorum brevis muscles of PPS patient and healthy subject. In the patient, the first 4 increments in the responses are shown (top, left) while in the control recording (top, right), there are 14 increments. See text.

years after an attack of poliomyelitis. In both subjects, stimuli were applied to motor fibers in the deep peroneal nerves, and the intensities gradually increased above the respective threshold values; the muscle responses were seen to grow in discrete increments, each of which represented the excitation of an additional motor unit. From a sample of 10 or more increments, the mean amplitude of the motor unit potentials could then be calculated and divided into the amplitude of the maximum muscle M-wave. In Figure 1, it can be seen that some of the increments were larger in the post-polio patient than in the healthy subject, and that the reverse was true of the maximum responses. While the larger motor unit potentials in the patient reflected collateral reinnervation by surviving motoneurons, the smaller maximum response indicated that there were fewer excitable fibers in the affected muscle than in the control. Of the 2 muscle studies shown in Figure 1, the post-polio patient was found to have approximately 17 motor units in his extensor digitorum brevis while the normal subject had 128.

The principle of comparing some parameter of the motor unit with that of the entire muscle can be extended to the area (voltage \times time) of the potentials [4] or to the sizes of twitches [5]. In our own laboratory, we have persisted with the original technique, based on motor unit potential amplitudes, largely because of its speed and convenience of execution; at the same

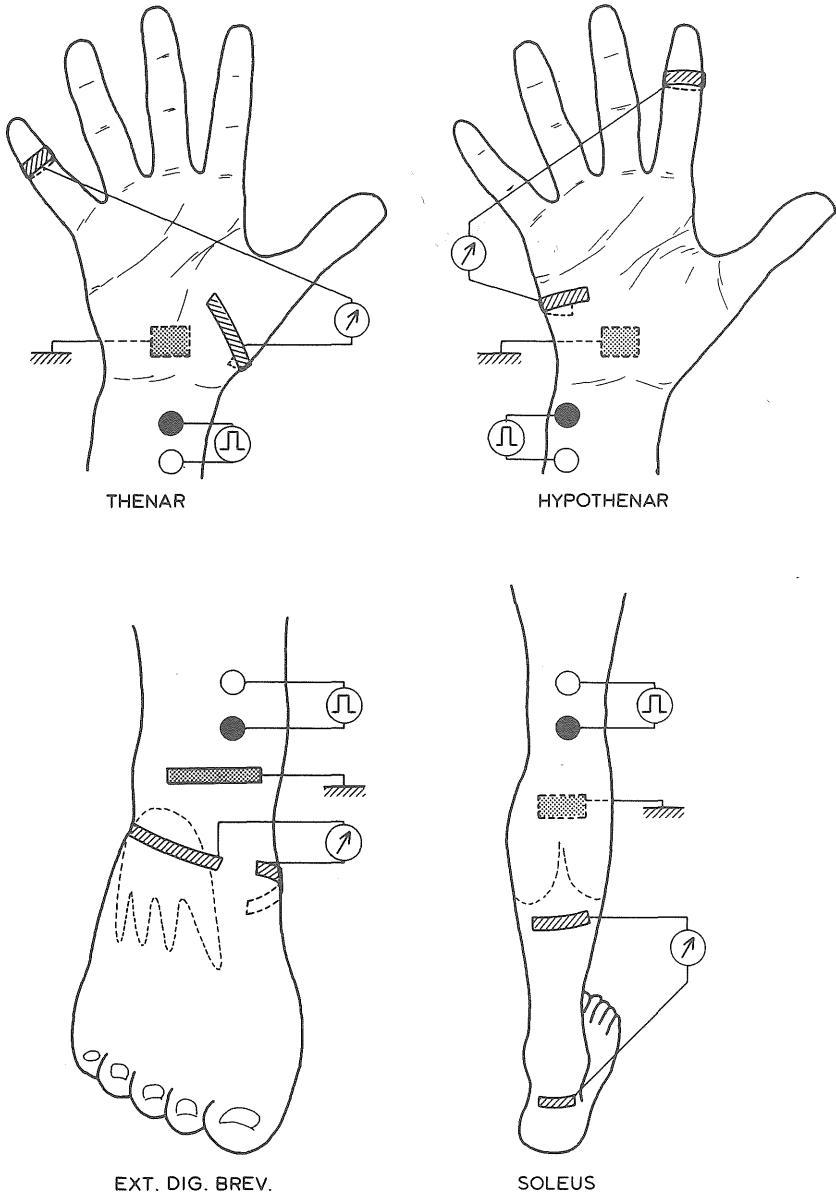


Fig. 2 Arrangements of stimulating and recording electrodes for counting motor units in the muscle groups most commonly employed for this purpose. ○, ● = anodal and cathodal stimulating electrodes, respectively. (From McComas AJ, Sica REP et al: Physiological estimates of the numbers and sizes of motor units in man. In Stein RB et al (eds): "Control of Posture and Locomotion." New York: Plenum Press, 1973, pp 52-72, with permission.)

time we acknowledge attempts to refine the methodology and, in particular, to deal with the troublesome problem of "alternation" [6].

Figure 2 shows the arrangement of stimulating and recording electrodes for the 4 muscles or muscle groups most frequently employed in motor unit counting. All 4 muscles have accessible peripheral nerves for stimulation, while the extensor digitorum brevis has the additional advantage of a single end-plate zone and a flat muscle belly; the soleus muscle, although far from ideal, is the largest muscle for which motor unit counting can be adapted. The mean numbers of the motor units, and the respective ranges of values found for these 4 muscles in a large population of healthy subjects, are given in Table 1. The numbers of functioning motor units have been found to remain relatively constant until the end of the sixth decade, after which they progressively decline [8]. This reduction is greater in the 3 distal muscles (extensor digitorum brevis, thenar, and hypothenar) than in the more proximal muscle (soleus) [9]. It is also larger than the loss of putative α -motoneurons determined by Tomlinson and Irving [10] in lumbosacral enlargements of cadaveric spinal cords. This last discrepancy has been attributed to differences between proximal and distal muscles and to the relatively demanding nature of the electrophysiologic criteria; thus, not only must motoneurone somata be present, as in the anatomic studies, but their axons must be capable of exciting colonies of muscle fibers.

The motor unit counting technique has an appreciable methodologic error such that the coefficients of variation, even under optimal conditions, range from 8% to 15% (Sica and McComas, unpublished). In addition, there are uncertainties regarding the adequacy of the sample of motor units from which the mean potential amplitude is derived as well as problems due to overlapping thresholds of motor axons (alternation). Despite these reservations, the method has proved indispensable in the diagnosis of muscle denervation in the EMG clinic and is far more sensitive than automatic analysis of volitional motor unit potentials, as recorded in the conventional way with a coaxial needle electrode [11].

TABLE 1. Electrophysiologic Estimates of Numbers of Motor Units in Human Muscles*

Muscle	No. of Motor Units (mean \pm SD)	Range	No. of Observations
Extensor digitorum brevis	210 \pm 65	120-414	151
Thenar†	342 \pm 97	220-693	115
Hypothenar	390 \pm 94	250-734	109
Abductor pollicis longus	421 \pm 99	272-666	40
Soleus	957 \pm 254	542-1579	41

*From McComas AJ: "Neuromuscular Function and Disorders." Boston: Butterworths, 1977, with permission [7].

†Median innervated.

The power of the method can be gauged from Figure 3 in which the numbers of functioning motor units have been determined in the intrinsic muscles of the hand and foot in patients with amyotrophic lateral sclerosis (ALS) at the time of diagnosis. It can be seen that, overall, the motor unit estimates were reduced in 224 of the 236 muscles sampled. Further, in some of the muscles having normal numbers of units at the initial examination, profound reductions could be demonstrated 3 to 6 months later. These last results stand in contrast to those of adult patients with spinal muscular atrophy in whom the motor unit counts, although reduced, remain remarkably constant over periods as long as 10 years [12].

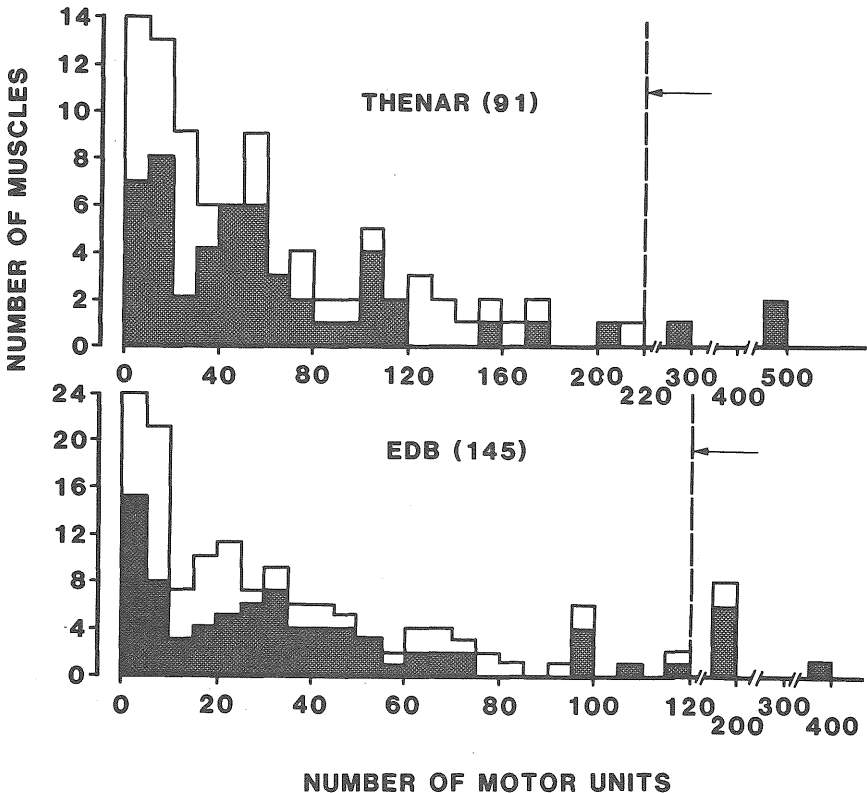


Fig. 3. Numbers of functioning motor units in 236 intrinsic muscles of the hand and foot in patients with ALS; only observations made at the time of diagnosis have been included. Vertical bars indicate lower limits of respective control ranges. Open and filled columns indicate values for patients above and below the age of 60 yr, respectively. Modified from McComas, 1987, [12] with permission.

TEST 2—TWITCH INTERPOLATION

While the first test, reported above, is clearly directed at the lower motoneurone, the purpose of the second test is to examine the functional integrity of the descending motor pathways. The principle of the test is to introduce a single maximal stimulus to the motor nerve while recording the torque developed by a muscle during maximal voluntary contraction. In theory, if some motoneurons have not been recruited, or else are firing at a suboptimal rate for tension development, the effect of the indirect stimulus will be to superimpose a twitch on the recording of maximal voluntary torque. The simplest test of the method is to require a healthy subject to make a series of contractions of increasing intensity; as shown in Figure 4, a point is eventually reached at which the twitch can no longer be recognized even with additional amplification. This result has been shown to be true of the dorsiflexor muscles of the ankle [13], quadriceps femoris, adductor pollicis [14], and the diaphragm [15]. In contrast, full motor unit activation is not always possible during contractions of the plantar flexor muscles [13]; however, it appears that the motoneurons with high thresholds for isometric contractions may be activated quite readily in sudden phasic movements [16].

Two of the patient groups to which the twitch interpolation technique has been applied are those with limb girdle muscular dystrophy and myotonic muscular dystrophy. In both populations, some patients with moderately severe weakness were encountered in whom there was evidence of incomplete motor unit activation, even in the ankle dorsiflexor muscles. This deficiency appeared to be dysfunctional inasmuch as full activation could be achieved eventually by repeated attempts accompanied by strong encouragement [17, 18].

TEST 3—PROLONGED REPETITIVE STIMULATION

Repetitive indirect stimulation of muscles has long been used as a method of testing neuromuscular transmission and has therefore been particularly useful in the diagnosis of such disorders as myasthenia gravis and the Lambert-Eaton syndrome. However, largely because of the pain involved, stimulation is usually restricted to a few seconds, and there has been a recent tendency to use relatively low rates of stimulation. In an attempt to provide a more rigorous test of muscle fatigability, we have taken advantage of the low stimulus threshold of the peroneal nerve at the neck of the fibula. In addition, it has been possible to stimulate the ankle dorsiflexors to mechanical exhaustion while applying an arterial occlusion cuff. Relatively low repetition rates (15 Hz or 20 Hz) are preferred, using continuous or interrupted modes; such rates probably correspond fairly closely to motoneurone discharge

PLANTARFLEXORS

TA/DORSIFLEXORS

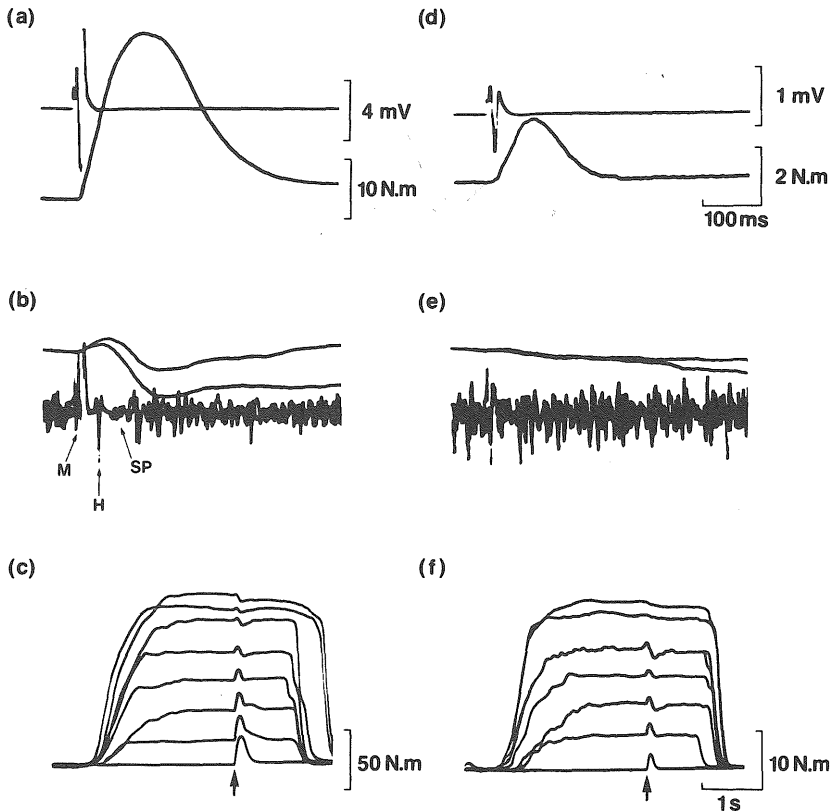


Fig. 4. Interpolated twitch technique in ankle plantar-flexor and dorsiflexor muscles. (a) and (d) show maximal resting twitches with associated M-waves (upper traces). In (c) and (f), subject made increasingly strong voluntary contractions; interpolated stimuli, delivered at moments indicated by arrows, evoked progressively smaller twitches as voluntary contraction intensified. In (b) and (e), the responses to interpolated stimuli during maximal contractions have been enlarged; a small twitch is evident for the plantar flexors but not for the dorsiflexors. EMG record also shows M-wave (M), H-reflex (H) and silent period (SP). (From Belanger AY, McComas AJ: Extent of motor unit activation during effort. *J Appl Physiol* 51:1131–1135, 1981, with permission.)

patterns during sustained effort [19] and minimize the muscle fiber excitation failure that is a feature of higher frequencies. Figure 5 shows an example of continuous stimulation at 20 Hz in a 52-year-old man; in addition to dorsiflexor torque, recordings have been made of the M-waves (muscle compound action potentials). The figure shows that the M-wave initially

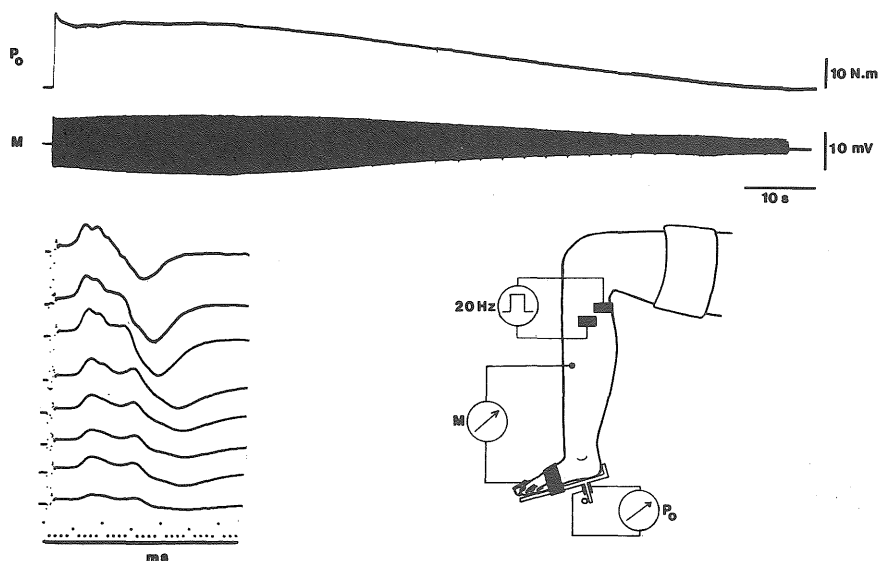


Fig. 5. Top: Responses of ankle dorsiflexor muscles to continuous maximal stimulation at 20 Hz while ischemic; P_o , tetanic torque; M, M-wave. Note initial enlargement and subsequent decline of M-waves, also seen in recordings taken at intervals during stimulation (bottom, left.)

increases in amplitude (and in area) before declining, while the reduction in tetanic torque is even greater, such that small M-waves can still be recorded at a time when the muscle is no longer capable of generating tension. When intermittent, rather than continuous, stimulation is employed, it is possible to record the isometric twitch as well (Fig. 6); the finding that the twitch can be abolished with little reduction in the M-wave points to the importance of impaired excitation-contraction coupling and/or contractile machinery failure in determining fatigue under relatively normal circumstances.

DISCUSSION—APPLICATION OF ELECTROPHYSIOLOGIC TESTING TO PPS

Three hypotheses may be considered to explain the weakness characteristic of PPS: 1) further loss of α -motoneurons; 2) defective activation of α -motoneurons; and 3) dysfunction of motor nerve twigs and muscle fibers.

Of these hypotheses, the first is perhaps the most attractive in view of the initial destruction of α -motoneurons by the polio virus and the further depletion known to occur as part of the normal aging process [8]. However, the loss due to aging does not normally appear before 60 years [3, 8, 10], and it would be necessary to postulate that the aging effect had been accentuated.

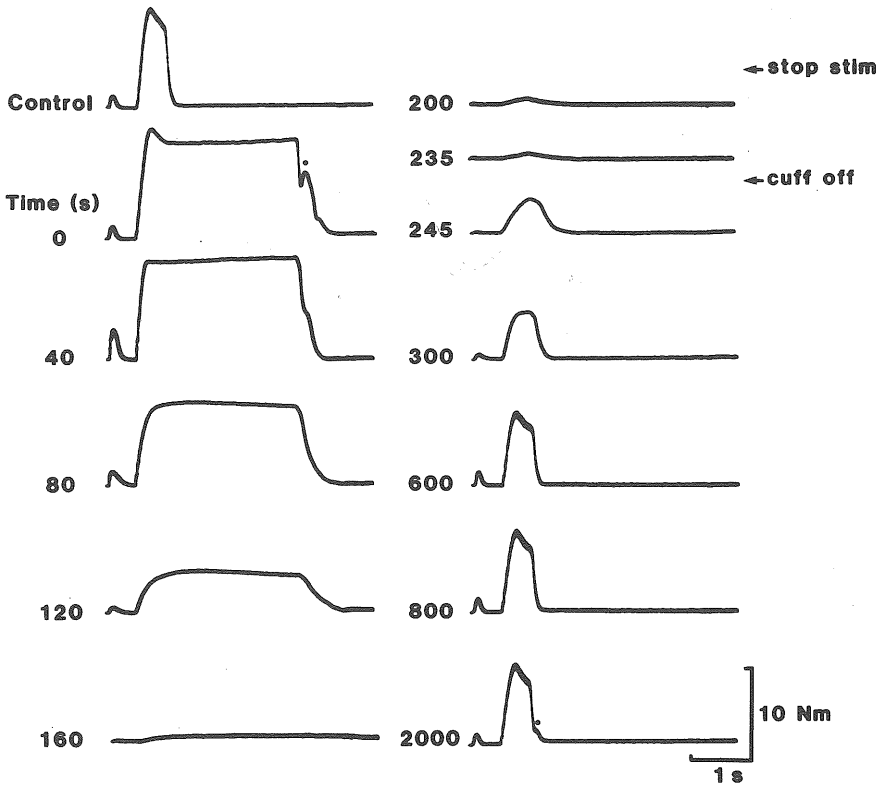


Fig. 6. Twitch and 30 Hz tetanic responses of dorsiflexor muscles at rest and during intermittent stimulation at 30 Hz under ischemic conditions; times (in seconds) shown beside traces. Notice potentiation of twitch at 40 s followed by gradual disappearance of evoked torque and then by recovery after stimulation was stopped and cuff released.

Although the latter might occur through persistent damage to the motoneurone following viral infection, the ability of surviving motoneurons to undertake collateral reinnervation of muscle fibers makes this explanation unlikely. Premature aging might come about, however, as a consequence of the extra metabolic demands imposed on the motoneurone soma by collateral reinnervation; such a mechanism has been proposed as a factor contributing to motoneurone degeneration in ALS [20].

The hypothesis of premature motoneurone degeneration in PPS is one that can be readily tested by serial motor unit counting, as has been done for ALS and spinal muscular atrophy. In view of the methodologic error (see above), it would be prudent to combine the results for all the muscles investigated on the same occasion in a single patient to determine an overall

motor unit quotient for that individual. To ensure experimental validity, tests would be conducted by the same observer and also be performed on age- and sex-matched controls free of neuromuscular disease.

At first sight, the second hypothesis, that of impaired motoneurone activation, is perhaps less plausible. There are, nevertheless, 2 reasons for exploring it. First, clinical signs of upper motoneurone involvement may occasionally develop during an attack of polio, raising the possibility of premature aging of upper motoneurons in later life. Second, incomplete activation of motoneurons has been noted in some patients with 2 types of muscular dystrophy [17, 18]. As noted earlier, full activation could be restored by repetition and motivation, an observation that suggests that the deficit in the dystrophic patient is dysfunctional and related to the transient decrease in motoneurone excitability found in otherwise normal subjects following a period of disuse [21, 22]. Irrespective of potential mechanisms, the possibility that motoneurone activation fails in PPS can be explored by the interpolated twitch technique.

The third hypothesis concerning PPS is that the weakness stems from a relatively subtle failure in the excitation or contraction of muscle fibers. On the basis of a comprehensive follow-up study, which included single fiber EMG and muscle biopsy, Dalakas et al [23] have suggested that PPS results from degeneration of individual motoneurone terminals rather than of whole motor units. In the investigation that we propose, such a situation would be revealed by serial studies in which the maximum M-wave would decline, although the motor unit count would remain stable. This combination of results has been noted in the stage of partial synaptic failure described by McComas et al [24]. If this explanation were correct, the results of prolonged tetanic stimulation should prove informative; dysfunction of motor nerve terminals should be revealed by unusually rapid decrements in the M-waves, as found in ALS and axonal neuropathies. Finally, the possibility of some change in excitation-contraction coupling or in the efficiency of the contractile machinery in PPS cannot be ruled out, in view of the secondary "myopathic" features that can supervene in muscles with chronic partial denervation [25]. In the study proposed, such a mechanism would be detected by unusually small torques relative to M-waves during repetitive stimulation.

In conclusion, PPS poses an interesting challenge to the clinical electrophysiologist; while partial answers may be derived from the utilization of conventional EMG procedures, it is hoped that more specialized techniques, such as those described here, may provide a more complete picture.

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Reinnervation After Acute Poliomyelitis

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From 1969 to 1980, 290 million doses of trivalent oral polio vaccine (TOPV) were distributed in the United States. According to the Center for Disease Control (CDC) in Atlanta, 25 vaccine-associated cases of acute polio were reported in TOPV recipients [1], and 55 cases of acute polio were reported in individuals who came in contact with the vaccinated individuals. An additional 12 vaccine-associated cases occurred in individuals with immune deficiency conditions. In 1982 and 1983, a total of 21 cases of acute polio were reported to the CDC, 9 cases in 1982 and 12 cases in 1983 [2]. Eight of these cases, who were among TOPV recipients, were all associated with the first dose, 9 cases occurred in individuals who were in contact with the TOPV recipient, and 3 cases occurred in immune-deficient individuals.

In this report, we will present the case of a TOPV recipient who developed the acute onset of paraplegia 23 days after receiving his first dose. In following the course of this child's recovery, electromyography (EMG) results have demonstrated that reinnervation by terminal axon sprouting continues for a much longer period of time than originally thought. During the child's most recent EMG exam at 21 months post-polio, almost all motor units continued to be unstable with repetitive discharge.

CLINICAL HISTORY AND RELEVANT LABORATORY INVESTIGATION

This child was exactly 2 months old when on July 2, 1984 he received his first dose of TOPV. On the afternoon of July 25, 1984, he became irritable with a weak cry and was noted to have a fever of 102°F. He was taken to a community hospital where it was noted he had a stiff neck and positive Kernig and Brudzinski signs. His fontanel was soft and examination of ears, nose, and throat did not reveal any inflammation. The remainder of his physical examination was normal. Laboratory examination demonstrated a sedimentation rate of 11, hemoglobin of 11.2 gm%, and a white cell count of 11,600 with 36 segmented leukocytes and 64 lymphocytes. A spinal tap revealed a chloride of 119 mg%, glucose of 48 mg%, with a serum glucose of 124 mg%, protein of

100 mg%, 10 white cells per mm³ of which 90% were lymphocytes and 10% polymorphonucleated leukocytes. Cultures of the spinal fluid grew no virus or bacteria. He was admitted with a diagnosis of viral meningitis. No weakness was noted, his fever began to subside, and he improved clinically over the next several days.

On July 29, 1984 it was noted that he was not moving his legs. His temperature was 99.2°F. Repeat spinal tap revealed a chloride of 116, protein of 96, glucose of 34, 28 red blood cells and 38 white cells of which 94% were lymphs and 6% polys. Spinal fluid cultures were again negative. Normal strength was noted in the upper limbs. Flaccid paralysis was noted in the lower limbs, with no movement in the left leg and less than antigravity strength in the right knee and ankle flexors and extensors. Sensation remained normal, but reflexes in the lower limbs were absent.

Clinical Course

The patient was first examined by the author on August 1, 1984. At this time, functional activity was noted in varying degrees in both ankle dorsiflexor and plantar flexor muscles, knee flexors, and toe flexors. Stool samples taken at this time and sent to the CDC eventually grew polio virus Sabin type 3. The patient was seen 28 days later, and antigravity strength was present bilaterally in these same muscles and also in the left hip flexor. Two months later, at age 5 months, the right hip extensor was of antigravity strength and the muscles initially functional on August 1, 1984 were now stronger than antigravity. At 4 months post-polio, the left hip adductor and left knee extensor became antigravity in strength.

At 6 months post-polio and 9 months of age, this child could sit if placed into the sitting position. He could roll from the supine position to prone but not the reverse. By 9 months post-polio and 12 months of age, the child's left hip extensors and right knee extensors became antigravity. At this time, he was able to crawl but dragged the right leg due to the absence of right hip flexion. He had developed greater than antigravity strength in the right hip extensors, the left hip flexors, left knee flexors and extensors. He could also sit independently. X rays taken at this stage revealed that his lower limbs were of equal length with normal development of the hips and pelvis. The pelvis, however, was tilted higher on the left, and there was a long curve of the spine to the right, implying that the paraspinal muscles might be involved.

At 14 months post-polio and 16 months of age, this patient regained antigravity strength in the right hip flexor and abductor, and his right knee extensor had become stronger than antigravity. Functionally, he was now able to crawl in a normal pattern using both lower limbs. He was also pulling to standing and could walk in the parallel bars with bilateral knee-ankle-foot orthoses and a left one-half inch heel and sole lift.

At the present time, 24 months post-polio, he still has no function in the left hip abductors and right hip adductors. Because of his growth and walking, this child's right hip flexors and left ankle dorsiflexors are no longer antigravity in strength. He wears a 1 cm left heel and sole lift and a left ankle foot orthosis. He can now climb and descend stairs with the aid of a rail and walk without the use of a walker.

Electrophysiologic Data

Obviously, over the past 2 years, this child's strength has been improving while at the same time he has been growing and developing. EMG of the leg muscles was initially performed at 4 months of age on August 29, 1984 and again at 24 months of age on April 21, 1986. The initial EMG was performed 4 weeks post-onset of paralysis with monopolar electrodes and a frequency response of 20 Hz to 10 KHz. The rectus femoris and anterior tibial muscles were examined bilaterally. Positive sharp waves and fibrillation potentials were profound. Only a few motor unit action potentials (MUAPs) of normal size were found in the left rectus femoris and left anterior tibialis and no voluntary MUAPs were seen in the right rectus femoris. Many normal sized MUAPs were seen in the right anterior tibialis. Left peroneal motor nerve conduction revealed a conduction velocity of 32 meters/second (m/sec) and an amplitude of 800 μ V.

At 21 months post-polio, a second EMG was performed, again with monopolar electrodes and a frequency response of 20 Hz to 10 KHz. Positive sharp waves and fibrillation potentials were present but did not seem as profuse as in the initial exam. The number of recruited MUAPs, however, varied from muscle to muscle. The right rectus femoris, which initially had no voluntary recruited motor units, showed many more MUAPs but continued to be markedly decreased from normal. The left rectus femoris, which initially had only a few functioning MUAPS, also showed a significant increase in units but a marked decrease from normal. The right anterior tibialis muscle continued to demonstrate a moderate loss of motor units. MUAPs recorded were of normal amplitude, 1–6 mVolts, of normal to long duration, from 4–14 m/sec, and most were polyphasic in shape. What was surprising was that essentially all MUAPs studied were unstable with repetitive discharge. Some MUAPs had complex polyphasic shapes of 4–8 m/sec in duration that changed dramatically with repetitive discharge (Fig. 1). Other MUAPs were of simple triphasic shape with late components that varied in their time of appearance following the main MUAP complex. On occasion, these late components would disappear only to return with the next depolarization of the MUAP. Many of these recordings were very similar to single fiber EMG recordings and some of the late components had the characteristics of individual muscle fibers despite the fact that the recordings were made with monopolar electrodes (Fig. 2).

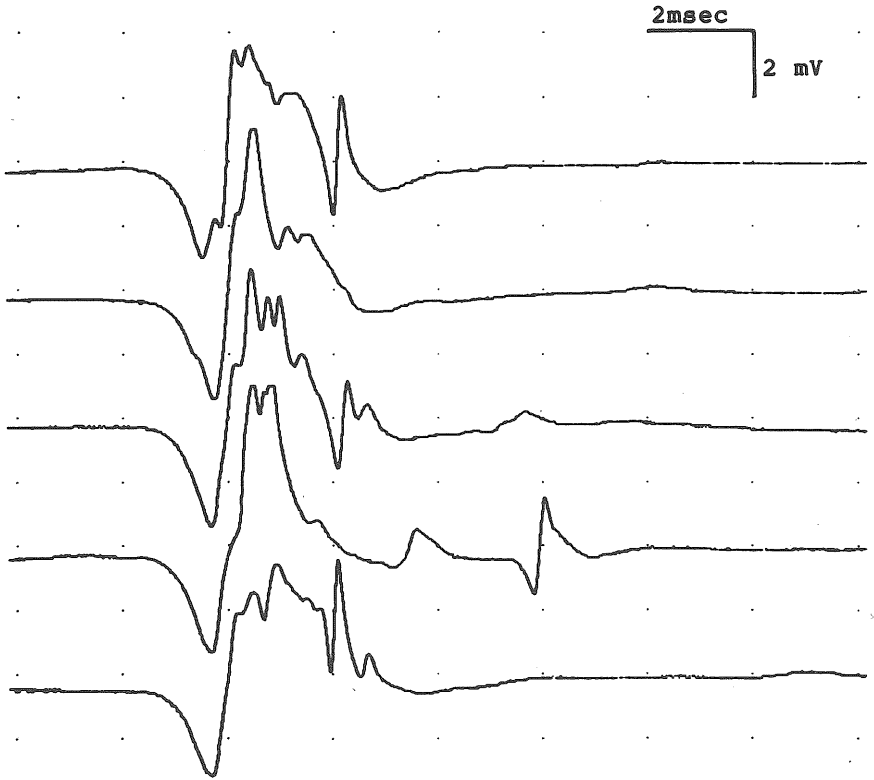


Fig. 1. Repetitive discharge of a motor unit action potential demonstrating instability of size and shape. Monopolar recording 20Hz–10KHz.

In some areas of the left rectus femoris, only one MUAP could be recorded. The potential, however, changed so dramatically in size and shape that it appeared to be groups of fibers or late components appearing and then disappearing in an all or none fashion. With continuing discharge and recording, these groups of fibers or grouped components of the MUAP could be seen moving back and forth and appearing and disappearing together within the whole MUAP complex (Fig. 3).

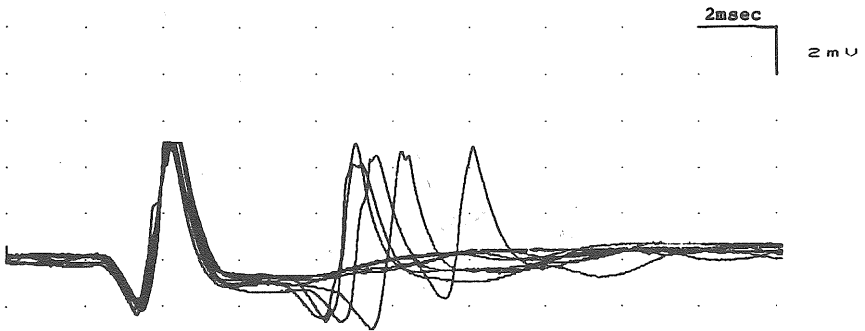


Fig. 2. Ten superimposed discharges of a reinnervating motor unit demonstrating transmission abnormalities. Monopolar recording yet characteristic of single fiber discharges with increased jitter and blocking. (20Hz–10KHz)

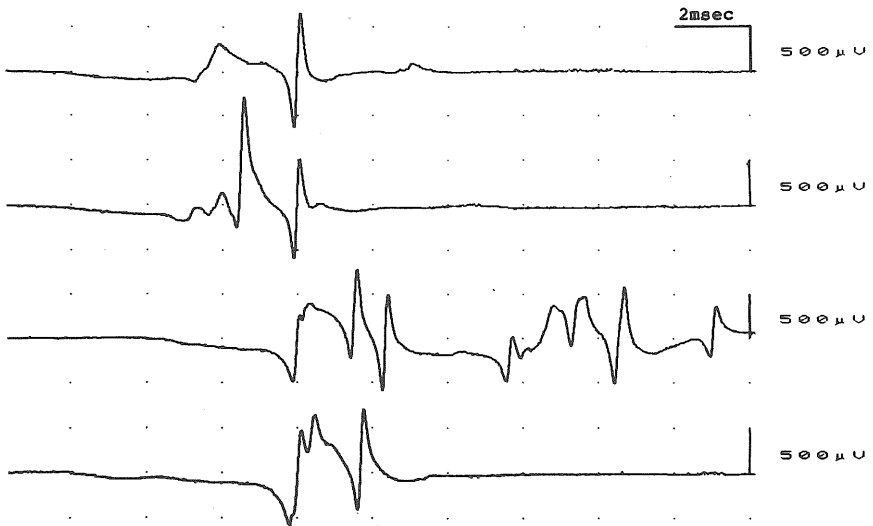


Fig. 3. Severe transmission abnormalities within this only functioning motor unit of the rectus femoris. Monopolar recording 20Hz–10KHz.

DISCUSSION

The instability of the MUAPs implies that transmission of the depolarization potential within the motor unit itself is abnormal. As demonstrated by single fiber EMG (SFEMG), the sites of these transmission abnormalities can be at the branching site of the terminal axon or anywhere along its length, at the neuromuscular junction, or along the individual muscle fiber.

The process of reinnervation by terminal axon sprouting occurs after polio [3]. As a result, a single terminal axon sprout may innervate a group of previously denervated muscle fibers. When the reinnervation process by terminal axon sprouting is active and ongoing, transmission frequently fails at the branching site of the axon sprout from the main axon trunk. As a result, whole groups of single fibers may not depolarize. On routine EMG, this would result in the sudden disappearance of a group of components of the whole MUAP in all or none fashion. In SFEMG, this is referred to as neurogenic blocking.

The term neurogenic blocking, then, is used to note that the transmission abnormality is at the branching site or in the terminal nerve and not at the neuromuscular junction or along the muscle fiber membrane. Transmission can also fail or be variably delayed along the immature axon sprout or at the new developing neuromuscular junctions that are being formed with previously denervated muscle fibers. In this instance, routine EMG recordings would demonstrate a change in size and shape of the MUAP with repetitive discharge. If the MUAP has late components, these may disappear individually or appear at variable delays from the main body of the MUAP.

In normal adult subjects, where free autogenous muscle is transplanted to the opposite side of the face following partial or total facial paralysis, MUAP stabilization in size and shape with repetitive discharge may be ongoing for 4 to 6 months [4]. In partial peripheral and root level nerve injuries, a 6 to 12-month period may be necessary for the MUAPs to stabilize, indicating that reinnervation by terminal axon sprouting is completed [5]. In conditions where there are many more denervated muscle fibers than can be reinnervated by the surviving motor units and especially in growing children or conditions affecting the motor neurons, the length of time that reinnervation by terminal axon sprouting may continue remains unknown.

The course of recovery and the electrophysiologic data in this child imply that reinnervation by terminal axon sprouting may continue for at least 2 years, and more than likely over a much longer period of time. It is also quite possible that motor neurons that are affected but survive the attack of polio may be delayed in their recovery and begin functioning again many months after polio. The process of reinnervation by terminal axon sprouting could then be found as demonstrated by motor unit instability at some locations within an affected muscle for extended periods of time. This long-standing

reinnervation and/or delay in return of function to motor neurons may be a factor in explaining why most post-polio patients state that they do not feel that they reached their maximal strength and state of functional recovery until 4 to 7 years post-polio.

Other possibilities exist for this continued motor unit instability that may also help to explain why motor unit instability is also seen in older polio patients regardless of whether or not they are having problems with the late effects of polio. In muscles where there are many more denervated muscle fibers than can be reinnervated by the surviving motor neurons, the individual motor unit may never stabilize. The motor neuron may constantly try to reinnervate more and more muscle fibers until it can no longer sustain all the fibers it has previously reinnervated. Some of these fibers may then fall away and the motor unit may remain in a constant state of remodeling.

The motor unit may also never stabilize because the desire of the motor neuron to reinnervate more and more muscle fibers is greater than its ability to supply them with consistent normal neuromuscular transmission. There is, without question, a limit to the metabolic capabilities of the motor neuron. In muscles where there are more denervated muscle fibers than can possibly be reinnervated, the surviving motor neuron may take on as many fibers as it possibly can, even though it cannot supply each with normal transmission. The motor neuron's goal may be to get as many muscle fibers functional as possible even though normal neuromuscular transmission is not established. There exists a safety factor to neuromuscular transmission of many μ /sec before the transmission fails, and no doubt, many periods of failed transmission are tolerated before the muscle fiber falls away from the motor unit. The motor unit may therefore be able to keep many additional muscle fibers functional simply by keeping the transmission less than normal but consistent enough to maintain connection.

Finally, the motor neuron that is affected but survives the attack of polio may be permanently scarred. It strives to reinnervate additional fibers, but its metabolic machinery is not capable of providing normal transmission to all of its reinnervated fibers.

Further studies on this child and on other post-polio patients will hopefully shed greater light on the concepts of reinnervation and motor unit function in post-polio and other motor neuron disorders.

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DISCUSSION

DR. JOHNSON: Did you do stimulation after one month to see whether a lot of these neurons were neuropraxic?

DR. WIECHERS: No, but obviously some neurons were neuropraxic because there was no function in some muscles right after onset and there was function after one month.

DR. FELDMAN: This brings up an interesting situation. Many years ago when I was a student, we came across a patient who was thought, at that time, to have polio who obviously had Guillian Barré syndrome (GBS). I am really wondering whether what we are looking at here is not just post-polio but perhaps other disease entities such as GBS or maybe peripheral nerve injuries that are going to react the same way after reinnervation. I wonder if you have any comments.

DR. WIECHERS: Are the late effects of polio only heralding us on to look for the late effects of GBS and other disorders? Yes, I feel that post-polio may become the model to study late effects of other disorders.

DR. DAUBE: To what extent were fibrillation potentials present at these reexaminations when you had unstable units?

DR. WIECHERS: Fibrillation potentials were quite profound at one month. At 21 months post-polio, it was very difficult to get the child relaxed enough to look at a normal base line, so I cannot say that quantitatively there was exactly the same amount of fibrillation potentials. However, between bursts of voluntary activity, there did not appear to be the profuse nature of fibrillation potentials and positive sharp waves as I had seen before function had returned.

DR. McCOMAS: I noticed that in some of the traces, the initial spike resembled later components in its amplitude and configuration. I was rather impressed by the traces and I wondered whether, in fact, there was some iterative firing going on, perhaps due to nerve twigs with low thresholds for excitation in responding to electric currents flowing in groups of fibers. Presumably, you could sort this out by just moving the needle a little bit and seeing whether the spikes change together or whether they dissociated.

DR. WIECHERS: That is an excellent point, and there is no reason to believe that some iterative firing is not also occurring. Do you think that would have some significance for this overall process?

DR. McCOMAS: Well, I think it is probably a sign of immaturity of some of the new twigs that are formed, inasmuch as that, for some reason or another, they have a much lower threshold to excitation, perhaps, partly to do with myelination. One must also take into account that the fibers are now forming in groups, and every time a motor unit discharges, there is going to be a much bigger field current flowing around the nerve twig that could produce its discharge. In animal muscles, the phenomenon of back-firing is well recognized although, even to date, the mechanism hasn't been finally established.

DR. BIELLIK: I think it would be valuable to give you some epidemiologic perspective on the incidence of vaccine-associated cases. For those who are not aware, a wild virus has not circulated in the United States probably since 1979, so that all nonimported cases of new acute polio in the United States are now vaccine-associated. Unpublished data at the CDC show that in both immunologically normal and abnormal persons combined, the incidence is now approximately one case of vaccine-associated polio per 3 million doses of vaccine distributed. But, this is divided between first dose and subsequent dose, and the incidence for first dose is more like one case per million doses distributed and subsequent dose—one per hundred million doses distributed. So, it is a first-dose phenomenon, but second-dose vaccine-associated cases are not unknown but are rather very rare. We have been discussing the possibility of collecting together a large number of these vaccine-associated cases from recent years, for which we have extensive data, and Dr. Wiechers is discussing the possibility of a prospective study of a large cohort of these cases over an extended period.

DR. DALAKAS: It is very important to look at patients with acute polio electrophysiologically and also by analyzing the spinal fluid. We have contacted the people in Taiwan; there is an electrophysiologist there who has done some earlier electrophysiologic studies 4 or 5 years after an outbreak of polio in Taiwan. He has reported to us that he has found fibrillations and instability of motor units up to 5 years in patients that he has studied so far. However, there is variability from patient to patient and from muscle to muscle even in the same patient, according to the reports that he has sent us.

DR. WIECHERS: Well, I think that these findings are very crucial. Many of the polio patients tell us that they didn't reach their maximum point of recovery for 7 or 8 years. So, it is quite possible that this reinnervation process after polio is quite different. When we think of nerve injury or muscle transplant reinnervation, normally it proceeds to completion in less than a year. Reinnervation after polio may go on for many years and would explain why the polio patients state that they really didn't reach their maximum point of recovery for 7 or 8 years following polio.

Late Effects of Poliomyelitis on Muscular Function and Morphology: A Preliminary Report

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An increasing number of patients who suffered from acute poliomyelitis 30 to 40 years ago are developing new muscular symptoms such as fatigue, weakness, pain, or fasciculations [1, 2]. The pathogenesis is unknown, and a desire to study muscular function and muscular structure in these patients originates from data presented at The First Research Symposium on Late Effects of Poliomyelitis in 1984 at Warm Springs, Georgia [3]. In a joint study between The National Society Against Poliomyelitis and The State University Hospital, Denmark, the muscular strength, gross morphology, and histology were evaluated in 10 patients who had acute poliomyelitis from 1946 to 1952.

PATIENTS

The group comprises 10 patients with symptoms of the late effects of poliomyelitis who have been selected according to the following criteria: 1) acute poliomyelitis in one leg (musculus quadriceps), and sparing or negligible involvement of the opposite leg; 2) independence from ambulatory aids for 30 to 40 years; and 3) sudden or gradual onset of fatigue, weakness, pain, or fasciculations in the formerly well-compensated leg.

METHODS

In all patients the following historical information was obtained. Present complaints were noted regarding onset, duration, influence on daily life, need

for ambulatory aids, decline in walking distance, stair climbing, rising from sitting to standing, car driving, and influence on employment and family. For the episode of acute poliomyelitis, the age at onset, severity, length of hospital stay, degree and duration of pareses, and former medical and surgical history were recorded. Patient characteristics are summarized in Table 1.

Several clinical and laboratory tests on muscular function and morphology were performed. The quadriceps muscle strength (graded 1–5) and the degree of atrophy (thigh circumference) were examined. The muscular volume and gross anatomy were also evaluated by computer tomography of both thighs at the same level that a needle biopsy was taken. Frozen sections of the muscle biopsies were stained with H&E, van Gieson, ATPase, NADH, α -glycerophosphate dehydrogenase, PAS, and reticulin. The bone mineral content of the lumbar spine, the femoral shafts, and the proximal part of the tibia was measured by dual photon scanning.

RESULTS

Results of the clinical evaluation of muscle strength and atrophy are outlined in Table 2.

Computer tomography was performed in 10 patients. Six showed muscular atrophy of the paretic leg. The isolated bundles of muscle tissue had normal density, indicating that adipose tissue was absent. Between the muscle bundles, strands of fatty tissue had counterbalanced the muscular atrophy so that the circumference of the paretic thigh was approximately equal to the circumference of the opposite thigh (Fig. 1).

Needle biopsies were taken from the lateral vastus muscles in 6 patients. In 2 patients, neurogenic atrophy was prominent in the paretic muscles, whereas slight type II fiber atrophy or normal morphology was encountered

TABLE 1. Characteristics of Post-Polio Patients

Patient No.	Current		Onset of Polio		Hospital Stay (Months)	Late Effects of Poliomyelitis	
	Age	Sex	Year	Age (yrs)		Year of Onset	Years Until Onset
1	42	F	1944	13	3	1985	41
2	38	F	1952	4.5	6	1981	29
3	42	F	1952	8	0	1981	29
4	72	F	1929	15	6	1984	55
5	38	F	1952	4	6	1984	32
6	55	F	1935	3.5	6	1985	30
7	43	M	1946	4	1	1984	38
8	42	F	1945	2	0	1985	40
9	37	F	1952	3	3	1985	33
10	68	F	1952	34	6	1985	33

TABLE 2. Clinical Evaluation of Muscle Strength and Atrophy

Patient No.	Femur Circumference		Atrophy in Polio Leg (cm)	Strength of Quadriceps	
	Right (cm)	Left (cm)		Right	Left
1	43	38.8	4.2	4+-5	3-4+
2	30	38	8	2-3	4
3	55.5	55	0.5	5	3
4	50	45	5	5	3
5	37.5	46	8.5	3	5
6	46	41	5	5	3
7	38	44.5	6.5	3	5
8	40	41	1	3	5
9	47	46	1	5	4
10	45	44	1	3	2

on the other side (Figs. 2 and 3). In another 2 patients, only minor atrophy of single type II fibers was seen in the paretic as well as in the clinically normal leg (Fig. 4). In the last 2 patients, the paretic leg was too atrophic to obtain any tissue, whereas their opposite legs revealed severe signs of neurogenic group atrophy with small type II fibers and type I fiber regrouping (Fig. 5).

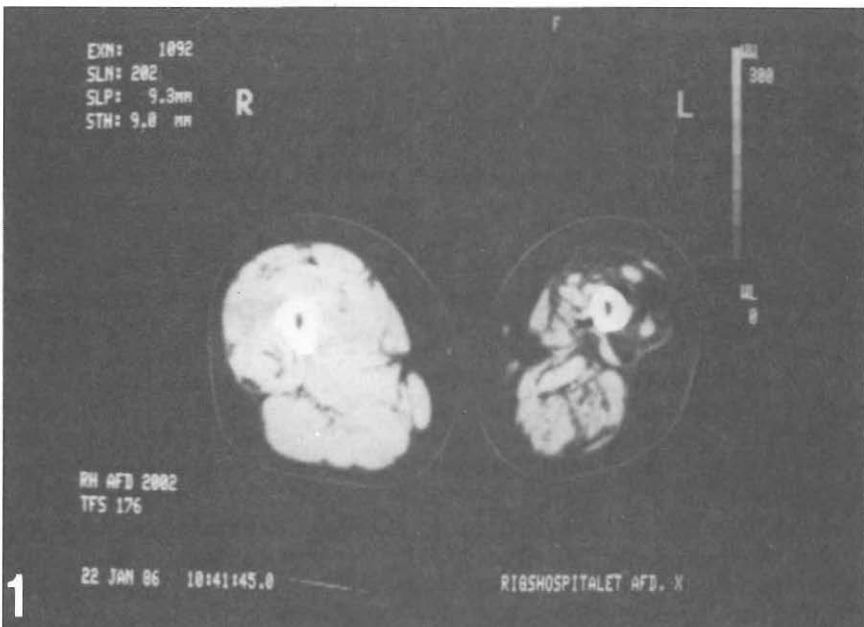


Fig. 1. Computer tomography of both thighs showing hypodense strands of fatty tissue replacing muscular tissue in the paretic leg.

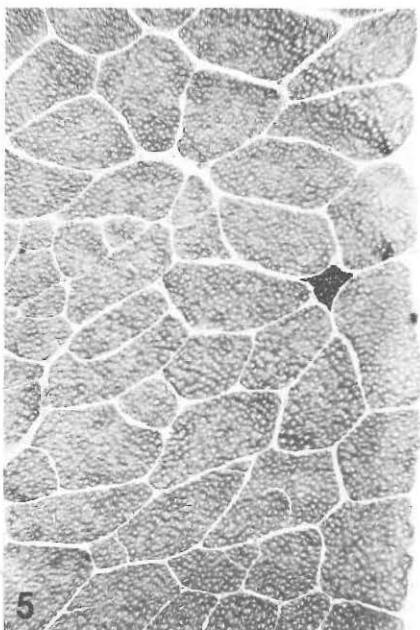
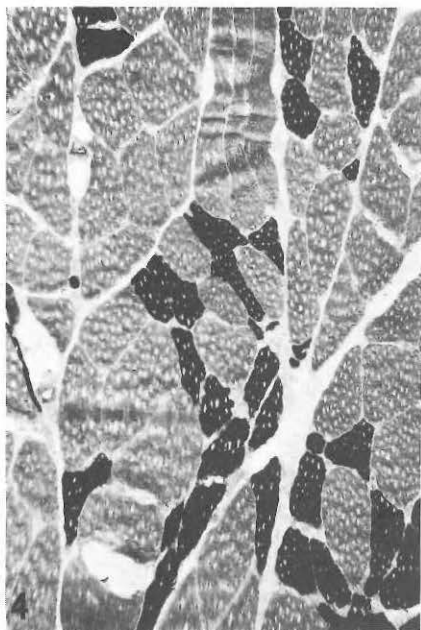
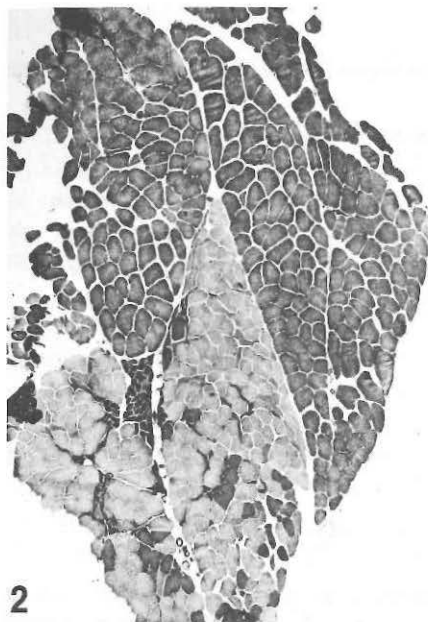


Fig. 2. Type II fiber neurogenic group atrophy and fiber type regrouping in paretic leg (NADH stain, $\times 35$).

Fig. 3. Same as Fig. 2. Dark fibers are type II fibers and light fibers are type I fibers (α -glycerophosphate dehydrogenase stain, $\times 140$).

Fig. 4. Type II fiber atrophy in paretic leg. Small isolated and angular dark fibers (ATPase stain, pH 10.3; $\times 140$).

Fig. 5. Type I fiber regrouping in leg without clinical paresis or symptoms related to late effects of poliomyelitis. An isolated angular dark type II fiber to the right (ATPase stain, pH 10.3; $\times 140$).

Inflammatory infiltration, degenerative or regenerative changes, vasculitis, connective tissue and fatty infiltration were not found in any of the biopsies.

The dual photon scanning in 5 patients showed a marked decrease in bone mineral content at about 20% to 50% in the leg affected by acute poliomyelitis. Finally, the laboratory findings did not indicate any signs of inflammatory or immunologic causes for late effects of poliomyelitis.

COMMENTS

We have examined 10 patients with late effects of poliomyelitis. Computer tomography and muscle biopsies showed atrophic and often profound changes, not only in the paretic legs, but also in the clinically normal legs. The bilateral involvement has been suggested previously by Hayward and Seaton [4], who found grossly raised mean amplitude of the interference patterns in many strong muscles as well as in weak muscles in an electromyographic study. Reinnervation indicated by fiber grouping and isolated, atrophic angulated fibers in previously recovered and newly affected muscles has been described by Dalakas and co-workers [5], who also observed perimysial and perivascular lymphocytic infiltrates. On the other hand, they did not observe group atrophy. The group atrophy in our investigation may indicate that neuronal involvement is more profound in late effects of poliomyelitis than suggested by Dalakas and co-workers.

A marked decrease in bone mineral content was observed in the paretic legs, although none of the patients had used a cane. Our clinical examinations, laboratory tests, and muscle biopsies have not offered any inflammatory or immunologic explanation for the late effects of poliomyelitis.

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Pathology of Spinal Cord in Post-Poliomyelitis Muscular Atrophy*

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INTRODUCTION

Paralytic poliomyelitis is an acute, self-limiting, motor neuron disease caused by the poliomyelitis virus types I, II, and III [1]. After the acute attack, patients recover or are left with a residual motor deficit. Although acute poliomyelitis is a monophasic disease, many years later, some patients develop a new, slowly progressive muscle weakness referred to as post-poliomyelitis progressive muscular atrophy (PPMA) [2, 3]. Based on the clinical, electrophysiologic, and muscle biopsy findings, we have previously hypothesized that PPMA is not due to death of the whole motor neurons, as in amyotrophic lateral sclerosis (ALS), but due to dysfunction of the surviving motor neurons, which can no longer maintain the metabolic needs of their distal axonal sprouts [2, 3]. Examination of the post-polio spinal cords could substantiate this hypothesis and provide insights into the status of motor neurons that survived a viral insult and, after years of compensation, have started to decline.

In the present study, we report the clinicopathologic findings in 7 post-polio patients who died from nonneurologic causes 9 months to 44 years (average 35 years) after the original illness. We specifically sought to examine changes in the spinal cord in asymptomatic post-polio patients as well as patients with PPMA in an effort to understand the evolving changes of the surviving motor neurons in relationship to the clinical symptomatology.

MATERIAL AND METHODS

We initially reviewed the medical records of 52 patients with old polio who had died from a variety of illnesses. Based on the available clinical

*The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as representing the views of the Department of the Army, the Department of the Air Force, or the Department of Defense.

information, however, only 7 post-polio patients were selected for review of their spinal cords. The other patients were excluded a priori either because the history of poliomyelitis had not been adequately documented or because another concurrent illness, ie, Alzheimer disease, various injuries, radiculopathies, or severe and chronic medical illness, could have possibly altered their spinal cord pathology. Patients above the age of 65 were also excluded to avoid changes in the spinal cord as an effect of aging [4].

The selected patients, aged 36–61 years at the time of death, had survived their paralytic disease from 9 months to 44 years (mean 35 years). All the patients (data summarized in Table 1) had a history of acute febrile paralytic illness in childhood or adolescence with partial recovery of motor function and subsequent stability. Most had contracted polio during the later epidemics of 1950 to 1952 when the diagnosis of poliomyelitis was made more accurately. One patient, (No. 6, Table 1) had polio in 1938 during a period of a neighborhood and school epidemic.

Four of the patients were asymptomatic (in reference to their neuromuscular system) at the time of death, with stable residual muscle weakness and atrophy in several limbs but no new weakness. Two patients (Nos. 5 and 6) had typical PPMA.

Six micron transverse sections of paraffin-embedded spinal cord from the cervical, thoracic, and lumbar regions were selected at random from all the patients. Sections were examined with H and E, Bodian's stains for axons, and Cluver-Barrera and Woelcke stains for myelin.

RESULTS

As expected, the brunt of the pathologic process was on the anterior horn cells, with the cervical and lumbar segments being more severely affected. Neuronal loss, atrophy of the surviving motor neurons, and active or inactive gliosis were present in all cases (Table 2 summarizes the main pathologic findings). Meningeal and parenchymal lymphocytic infiltration was seen in almost every case, decreasing with time (Fig. 1).

In one patient who died 9 months after the acute paralytic disease, in addition to perivascular and parenchymal lymphoplasmal cell infiltration, occasional glial nodules and neuronophagia were seen (Fig. 2). Another patient 5½ years post-polio had a unilateral hemorrhage and infarction of the anterior gray matter of the spinal cord.

Of interest was the pathologic changes in the 2 patients (Nos. 5 and 6) who were clinically typical of PPMA. In these patients, in addition to the above changes, occasional neurons with chromatolysis and numerous axonal spheroids were found (Fig. 3). These findings are indicative of a dynamic affection (disorder) of the anterior horn cells (see below). The spinal white matter was mildly gliotic in 2 patients. There was no evidence of corticospinal

TABLE 1. Summary of Clinical Findings in 7 Post-Poliomyelitis Patients

Patient	Age*	Sex	Post-Polio/Years	Clinical Status
1	36	M	3½	Complete paralysis with head and neck involvement. On respirator 'til his death.
2	44	F	5½	Complete paralysis from neck down. Most of her life on respirator.
3	44	M	¾	Paraplegia, subsequently improved with residual monoplegia. Atrophy left side of thorax. On respirator 'til his death.
4	46	F	23	Paraplegia since age 23, no new neurologic symptoms.
5	59	M	29	Stable post-polio. One year prior to death, developed pain and new weakness in his lower limbs (PPMA).
6	61	F	44	Stable post-polio until 2 years before death, when new upper and lower limb weakness developed (PPMA).
7	58	M	31	Stable post-polio with no new symptoms.

*Age at death.

tract involvement. The anterior nerve roots were atrophic and almost non-recognizable.

DISCUSSION

The most striking findings in our study were the presence of gliosis, inflammation, neuronal atrophy, and axonal spheroids in the spinal cords of all the post-polio patients examined from 9 months to 44 years (mean 35 years) after the original illness. These changes were unrelated to the presence of new symptoms, suggesting that in the post-polio spinal cord (the site of the original viral infection), a smoldering ongoing activity continues for many years after the acute attack.

Acute poliomyelitis is a monophasic disease characterized by severe inflammation, neuronophagia, active gliosis, and destruction of the anterior horn cells as described from spinal cords obtained from patients who succumbed during the height of their illness [1]. As in every acute, self-limiting viral illness, the inflammation and gliosis were expected to stop shortly after the acute infection had ceased. Our finding of perivascular and parenchymal inflammatory cells in post-polio patients suggests lymphoid cell hypersensitivity or involvement of cell-mediated immune mechanisms that continue many years after the acute viral insult. Poliomyelitis virus, an RNA virus, is usually cytolytic; however, it can cause a persistent infection in animals and immunosuppressed humans [5, 6]. Theoretically, residual of the poliovirus genome in neuronal and glial cells could trigger an attack on them by slow recruitment of cells of the immune system, leading eventually to dysfunction of the neurons. Whether the described inflammation in the

TABLE 2. Pathologic Changes in the Spinal Cords of Post-Poliomyelitis Patients

Patient	Age*	Sex	Post-Polio/Years	Loss	Neurons		Gliosis	Inflammation, Lymphocytic	White Matter Gliosis	Nerve Root Atrophy
					Atrophy	Neuronophagia				
1	36	M	3½	4+	+	—	3+ Active	2+	+	+
2	44	F	5½	3+	3+	—	3+ Active	2+	+	+
3	44	M	¾	3+	2+	? Glial nodular	4+ Active	4+	+	+
4	46	F	23	4+	+	—	2+ Inactive	2+	—	+
5	59	M	29	2+	2+	—	2+ Active	+	+	+
6	61	F	44	3+	2+	—	4+ Active	+	Gliotic	+
7	58	M	31	3+	2+	—	4+ Active	+	—	+

*Age at death.

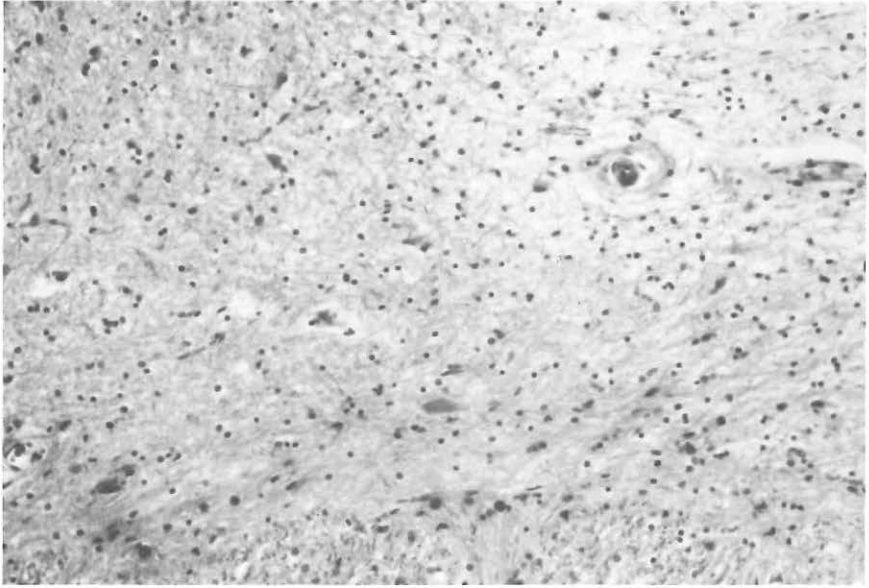


Fig. 1. Post-polio spinal cord showing sprinkles of lymphocytes in the gray matter. Neuronal atrophy and loss and mild active gliosis are also present (H&E $\times 15$).

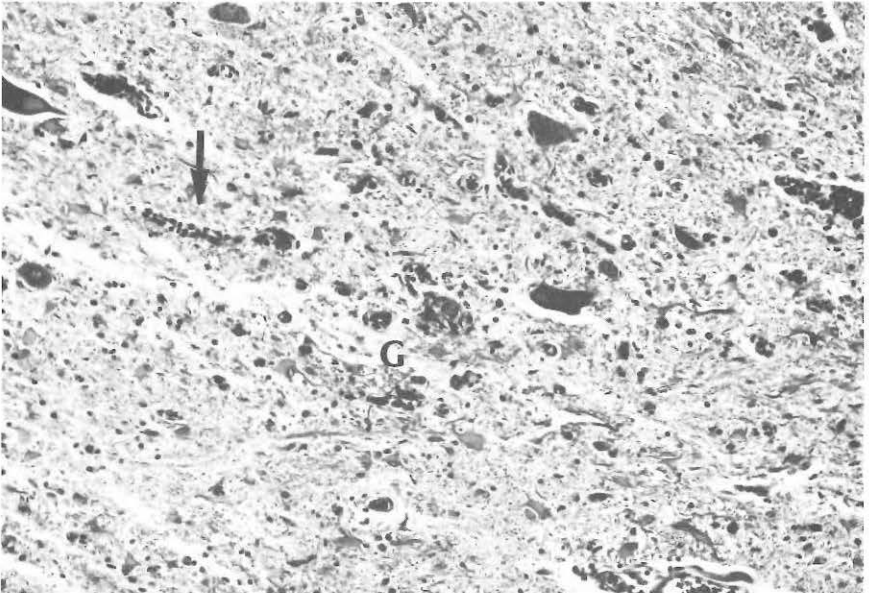


Fig. 2. Post-polio spinal cord, 9 months after the attack. Inflammation (arrows) and glial nodule (G) indicate continued disease activity (H&E $\times 80$).

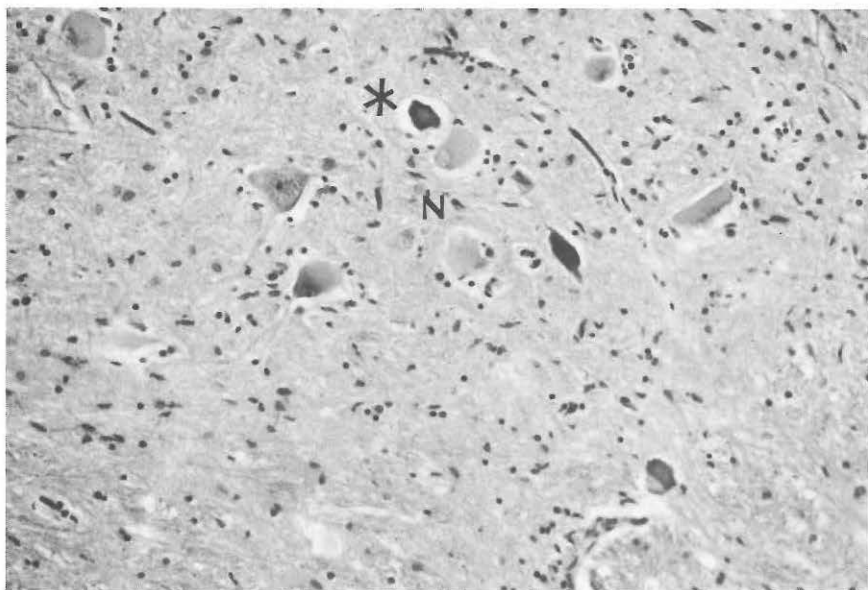


Fig. 3. Post-polio spinal gray matter in patient with PPMA showing chromatolytic neurons (N) and axonal spheroids (*) (H&E $\times 160$).

post-polio state suggests such a persistent viral activity due to viral particles that escaped the immune surveillance is unknown at the moment. Future experiments with *in situ* hybridization to look for possible residual viral genomes could provide answers to these questions, and they are now in progress.

Neuronal atrophy, axonal spheroids, and active gliosis were clearly more prominent in patients Nos. 5 and 6, who had new muscle weakness and appear to represent the pathologic basis of PPMA. The presence of atrophic neurons is consistent with our hypothesis that PPMA is due to dysfunction—but not death—of the motor neurons that can no longer maintain the needs of their distal sprouts and have lost the capacity for further reinnervation. Axonal spheroids are seen in early and rapidly progressive cases of ALS [7]. Their presence in the spinal cords of only the PPMA patients further supports an ongoing neuronal dysfunction. Because axonal spheroids have been thought to represent a defect in the movement of trophic material down the body of the axon [8], their presence in PPMA neurons supports our view that these neurons cannot maintain the metabolic needs of their distal sprouts, with resulting disintegration of individual nerve terminals.

The described histopathologic findings in PPMA are different from those found in ALS, the prototype of motor neuron diseases where axonal spheroids are infrequent (except in acute rapidly progressive cases), gliosis is minimal, and degeneration of the corticospinal tracts is always present [9]. These

histologic differences reinforce the variance we have found in the clinical course, the muscle biopsies, the spinal fluids, and the electrophysiologic studies [10], and strongly support our view that PPMA does not lead to ALS, but is a benign form of motor neuron degeneration.

All the post-polio patients examined after 9 months to 44 years from the original illness had signs of new neuronal activity in their spinal cords regardless of the presence of new weakness. Spinal cords in patients with PPMA differ, therefore, only quantitatively from the asymptomatic post-polio state. In this regard, PPMA may be considered the end of the spectrum of an ongoing neuronal reaction that has not completely ceased after the acute insult, but continues many years later, slowly affecting the ability of the surviving neurons to maintain the integrity of their distal nerve terminals and their capacity for additional axonal sprouting. The clinical manifestation of new weakness could therefore represent the "tip of the iceberg" in those continuously dysfunctioning neurons.

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DISCUSSION

DR. DAUBE: Did you examine the cortical neurons for any evidence of involvement? What about the interneurons in the anterior horn? Were they equally affected? Finally, where there was polio muscular atrophy as you

defined it clinically, did you see anything in the biopsy that related directly to that atrophy that wasn't present elsewhere?

DR. PEZESHKPOUR: To answer your first question, no, we didn't look at the cortical neurons. As for the second question about the interneurons, one can more or less speculate that there appeared to be a depopulation. Regarding the third one, we had areas of the spine that were much less affected. For example, the thoracic vertebrae in almost all of these 7 patients was spared, or was not that badly involved. The abnormalities we saw were mostly in the lumbar and then in the cervical portions of the cord.

DR. BRADLEY: Have you done any T-cell lymphocyte markers to both confirm that the cells were lymphocytes and what variety; also, has any electron microscopy been performed looking for viral or virus-like particles?

DR. PEZESHKPOUR: We are almost sure they are lymphocytes, but we have not done any typing. No electron microscopy has been done as yet. We hope to get some cases of post-polio that are fresh and be able to do a sort of probing on the spinal cord to see if we can identify the RNA or DNA of the polio viruses in the spinal cord.

DR. McCOMAS: Obviously, one must accept your findings, but am I right in thinking that they are very different from the studies of David Bodian on primates, where he did inoculation and showed motor neurons apparently becoming sick and containing virus and then the virus being removed from the cell bodies and the inflammation dying down?

DR. PEZESHKPOUR: I have not read Dr. Bodian's entire publication. However I don't remember what he mentioned about the virus being removed from the nerve cell.

DR. JUBELT: I can comment. When he looked pathologically, most of the anterior horn cells were infected and about half of those died and about half went on to recover. After a year or so, they looked like they were normal. There was no longer any central chromatolysis, and the inflammation had resolved. So, as far as I know, he has never looked 10, 15, or 20 years after the infection.

You found differences in the glial cell response between patients who were and were not progressing, and I wanted to clarify. Was there any difference in the lymphocytic inflammatory response?

DR. PEZESHKPOUR: Inflammatory response in the PPMA group was much more severe than the nonprogressing group.

DR. JUBELT: Occasionally, we can see a little bit of inflammation in ALS patients, but this looks like it is much more than what you usually see in ALS patients. Is that right?

DR. PEZESHKPOUR: Yes, but very rarely in cases of very rapidly progressive ALS do you see a mild inflammatory response.

Post-Poliomyelitis Syndrome: Evidence of Ongoing Denervation in Symptomatic and Asymptomatic Patients

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New weakness, pain, and fatigue (post-polio syndrome, PPS) may affect 25% of patients with prior paralytic poliomyelitis [1, 2]. In order to define electrophysiologic and muscle biopsy features of PPS, we have compared patients with new weakness to patients without new weakness decades after polio [3, 4]. A subgroup of patients with new atrophy (post-poliomyelitis progressive muscular atrophy, PPMA) was also compared to patients without new atrophy [5]. All groups (weakening v control, newly atrophic v no new atrophy) were well-matched for age, severity of original poliomyelitis, and years since polio [3–5].

Consistent with remote polio, electromyographic (EMG) changes of chronic denervation were common in weakening and control patients [3, 4]. Unexpectedly, however, conventional EMG and single fiber EMG (SFEMG) also detected evidence of ongoing denervation in both weakening and control patients. Neither weakening patients nor patients complaining of new atrophy were discriminated from asymptomatic patients by SFEMG [5].

Muscle biopsy findings paralleled those observed with electrophysiologic techniques. Evidence of remote denervation of the original poliomyelitis was observed in every patient studied. Small angulated fibers, which are commonly associated with ongoing denervating diseases, were observed in virtually all patients [3, 4]. In contrast to a previous muscle biopsy study of patients with PPMA [6], approximately 50% of weakening and control patients exhibited group atrophy [3, 4], a putative sign of motor neuron disease, although also consistent with axonal branch degeneration in an extensively sprouted motor unit. Grouped atrophy was not significantly increased in patients with the clinical complaint of new muscle atrophy [5]. We found that fiber-type grouping on muscle biopsy, a consequence of remote

denervation of polio, is significantly correlated with grouped atrophy in the same biopsies, suggesting that motor units grossly enlarged by axonal sprouting in recovered poliomyelitis may undergo late degeneration. We have previously reported [3, 4] that electrophysiologic evidence of remote denervation (SFEMG fiber density) is correlated with degree of motor unit instability (increased SFEMG jitter). Immunohistochemical examination of muscle biopsies for expression of neural cell adhesion molecule (N-CAM) corroborated the presence of ongoing denervation in weakening and control patients [3, 4]. No biopsy feature distinguished newly atrophic patients from patients without new atrophy [5].

Our results indicate that reinnervation of denervated myofibers is not indefinitely stable, supporting Wiechers' and Hubbell's findings [7]. Compensatory reinnervation of denervated muscle fibers can markedly enlarge the territory of the motor unit. In the years following recovery from paralytic poliomyelitis, disintegration of outlying sprouts may denervate previously reinnervated muscle fibers [7], which may not be reinnervated by neighboring "healthy" axons extended to their limit by prior sprouting. Regeneration of terminal axons also may be less efficient with aging [8], increasing demands on the already critically enlarged motor units. Accelerated peripheral disintegration of sprouts and/or degeneration of motor neurons may follow.

Our data do not explain why only a subgroup of patients with a history of poliomyelitis develop PPS. We have found that no EMG, SFEMG, or muscle biopsy feature was significantly more common in weakening patients than in nonweakening patients [3, 4]. In addition, we found that patients complaining of new atrophy with weakness (PPMA) are not distinguishable from post-polio patients without new atrophy by SFEMG and muscle biopsy [5]. However, patients complaining of new atrophy tended to have PPS for more years than patients without new atrophy, suggesting that new atrophy is a late symptom of PPS [5]. Precipitants of clinical decompensation must be sought and modified to prevent or slow the "second disability" of PPS.

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New Neuromuscular Symptoms After Old Polio (“The Post-Polio Syndrome”): Clinical Studies and Pathogenetic Mechanisms

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INTRODUCTION AND HISTORICAL POST-POLIO PERSPECTIVES

About 5 years ago, we discovered that some patients with old polio were experiencing new neuromuscular symptoms, which the post-polio sufferers had named “post-polio syndrome.” Although neurologists have been aware for years that some patients with old polio may experience later in life progressive weakness in some of their already weak muscles [1–4], the term “post-polio syndrome” was not only new to us but also perplexing. Syndrome is a concurrence of a set of symptoms that occur together; in this context, we became interested in investigating the nature of the symptom complex within the so-called “post-polio syndrome.” Awareness of this very interesting “new syndrome,” along with my interest in motor neuron diseases, prompted us to start a careful examination of some of the post-polio patients with new symptoms.

From our first approach to a small number of such self-referred patients, it became apparent that within the eponym “post-polio syndrome,” patients had included a diverse group of symptoms and signs for which they had visited a number of physicians, including internists, gastroenterologists, orthopedists, neurologists, physiatrists, nutritionists, and psychiatrists. They had been given several different diagnoses, they were confused and angry because their true symptoms had not been adequately addressed or explained, and they were frustrated because no respected institutions or physicians were studying their problem. Others were frightened because their new symptoms resembled the original polio attack and were devastated by the possibility that poliomyelitis could return (a “second curse,” as some patients used to say). Within the “post-polio syndrome” group, the patients had included such a diversity of symptoms as pain, fatigue, weakness, headaches, paresthesias, constipation, back and neck pains, changes in their sleeping patterns, breathing difficulties,

hot and cold flashes, hypertension, bladder difficulties, and a series of gastrointestinal symptoms.

From our careful examination of the first group of post-polio patients, it was very clear that some patients had justified anxiety and fear. Others had musculoskeletal conditions such as degenerative arthritis or radiculopathies, compression neuropathies or other neurologic illness unrelated to polio, or new muscle weakness resulting from the old poliomyelitis that we called post-poliomyelitis progressive muscular atrophy (PPMA) [5–8]. Based on these preliminary observations, in 1982 we began a series of studies of patients with old polio who had started now to develop new neuromuscular symptoms. From 1982 until now, we have examined and thoroughly investigated a series of up to 60 such patients in an attempt to: 1) define the new symptoms and especially the new muscle weakness, 2) determine the rate of progression with several quantitative neurologic examinations, 3) understand the possible pathogenetic mechanisms via a series of histologic, electrophysiologic, immunologic, and virologic investigations, and 4) design effective therapies.

PATIENT SELECTION

All patients, who were studied after giving informed consent, had a history of acute paralytic poliomyelitis in childhood or adolescence. This was established by a careful review of records to document as well as possible the clinical occurrence of an acute febrile illness followed by paralysis. We checked for neighborhood or school epidemics, and we selected patients who were affected in the United States, particularly during the later epidemics, when the diagnosis of poliomyelitis was probably made with more accuracy. All patients were admitted to the National Institute of Neurological and Communicative Disorders and Stroke. They were either referred by their

TABLE 1. Estimated Points of Normal Neuromuscular Strength per Limb

Upper Limbs		Lower Limbs	
Right:		Right:	
Hand muscles:	5 points	Foot extensors:	5 points*
Wrist muscles:	5 points	Foot flexors:	5 points
Forearm extensors:	5 points	Knee extensors:	5 points
Forearm flexors:	5 points	Knee flexors:	5 points
Shoulder muscles:	5 points	Hip muscles	5 points
Total:	25 points	Total:	25 points
Left: total	25 points	Left: total	25 points
Total right and left =	50 points	Total right and left =	50 points
Total all 4 limbs = 100 points			

*5 points of normal total strength corresponds to 5 MRC scale of a muscle group; a decline from 5 points to 0 points of normal total strength corresponds to 5–0 points MRC scale, respectively, of that muscle group.

private physicians or were self-referred because they had begun to experience new muscle weakness. The patients enrolled in the study fulfilled the following criteria: They had partial recovery of motor function after polio and functional stability or recovery for at least 15 years; they had residual muscle atrophy, weakness, and areflexia in at least one limb but with normal sensation; and they had new muscle weakness and neuromuscular or musculoskeletal symptoms. Patients were excluded if they had diabetes, polyneuropathy, collagen vascular disease, exposure to toxic agents, other major viral illnesses, a family history of neuromuscular disease, or recent injuries in the back or neck. Only patients who were less than 60 years old at the initial visit (mean age, 42.7; range, 24–59) were entered in the study. This was done to exclude patients who were subject to a loss of motor neurons due to normal aging [9].

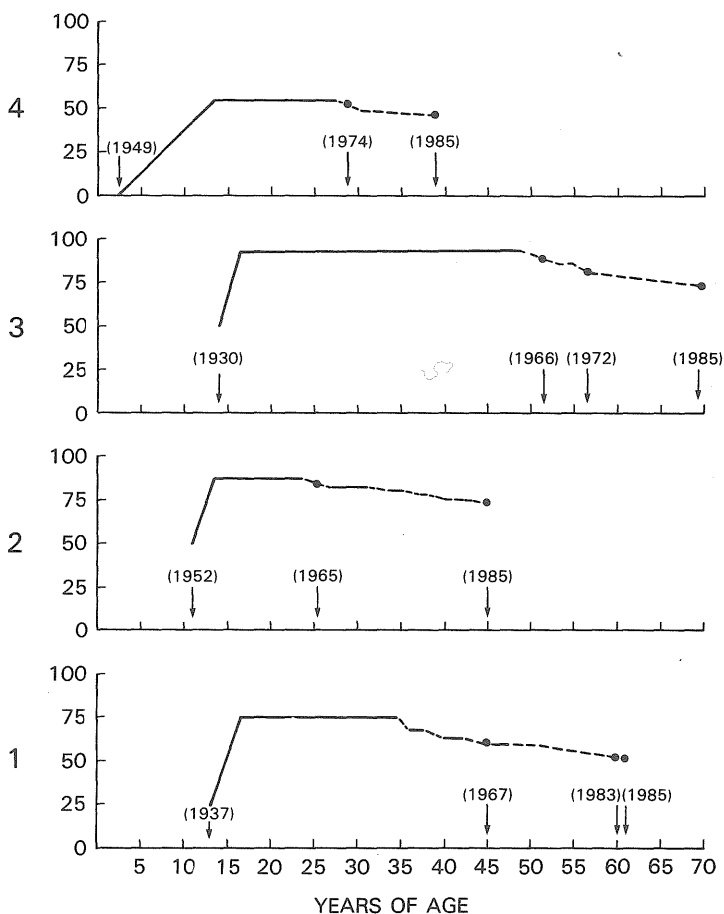
NEUROLOGIC EVALUATION AND FOLLOW-UP QUANTITATIVE STUDIES

All the patients were examined neurologically, and their muscle strength was quantitated according to the scale of the Medical Research Council [10]. The follow-up neurologic examination was performed in 27 patients to assess the rate of progression [7]. In addition to the patient's own descriptions of the functional decline in their muscle strength, we used an objective quantitative assessment of the newly developed muscle weakness based on the Medical Research Council rating for each muscle group in each limb. For this purpose, we used the following formulas presented in Table 1. We considered the total normal strength of the 4 limbs as 100 points of neuromuscular function and assigned 25 of those points to each of the 4 limbs. These 25 points were equally distributed among 5 major muscle groups (eg, in the leg, 5 points each were assigned to the foot extensors, foot flexors, knee extensors, knee flexors, and hip flexors and extensors). Five points of neuromuscular function for each of the major muscle groups corresponded to a "5" (normal) rating on the Medical Research Council scale. Weaker muscle groups that rated 4, 3, 2, 1, and 0 on the scale received 4, 3, 2, 1, and 0 points, respectively. These calculations provided an automatic estimate of the cumulative total strength of every limb. The points for the total strength that remained at the initial and subsequent follow-up visits were plotted against the age of the patient at those visits, as shown in Figure 1, and discussed below.

LABORATORY STUDIES

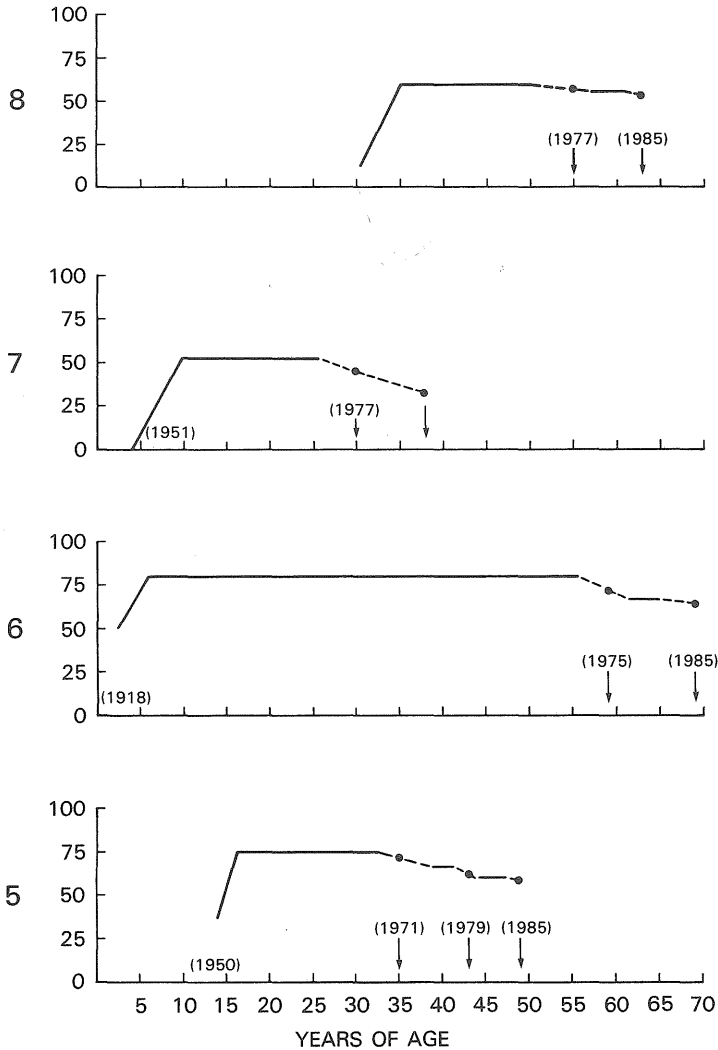
Blood Chemistry

These included routine studies and determination of muscle enzymes such as creatine kinase (CK), aldolase, aspartate aminotransferase, and alanine aminotransferase.



1a

Fig. 1 (a, b, and c). Progression of muscle weakness in 12 patients with post-poliomyelitis muscular atrophy, expressed as total points of estimated neuromuscular function at various years of age. Numbers on the left refer to individual patients. Points of muscular function (100 points is the normal strength in all 4 limbs) are on the ordinate. The continuous line represents the patients' course after the attack of acute polio and their progressive partial recovery with subsequent long stabilization, as determined from information provided by the patient or early records. The interrupted line represents the course of new muscle weakness from onset until the latest follow-up evaluation. Arrows with the year in parentheses represent the time of acute polio attack (first arrow), the time of the first examination after the manifestation of new weakness (second arrow), and subsequent examinations (third or fourth arrow). The sharp angulations in many of the curves are due to the subjective data on neuromuscular function provided by the patient. A decline in muscular strength that was either continuous or that occurred in a stepwise fashion took place in all 12 patients between the first and last evaluation (mean follow-up period, 11.6 years).



1b

Fig. 1 (cont'd)

Open Muscle Biopsies

These were performed on 27 patients with new muscle weakness and on 5 asymptomatic post-polio patients who served as controls. Post-polio muscles at different stages of residual deficit were studied. These included newly symptomatic or asymptomatic muscles that had fully or partially recovered after the original illness or muscles originally spared, according to available

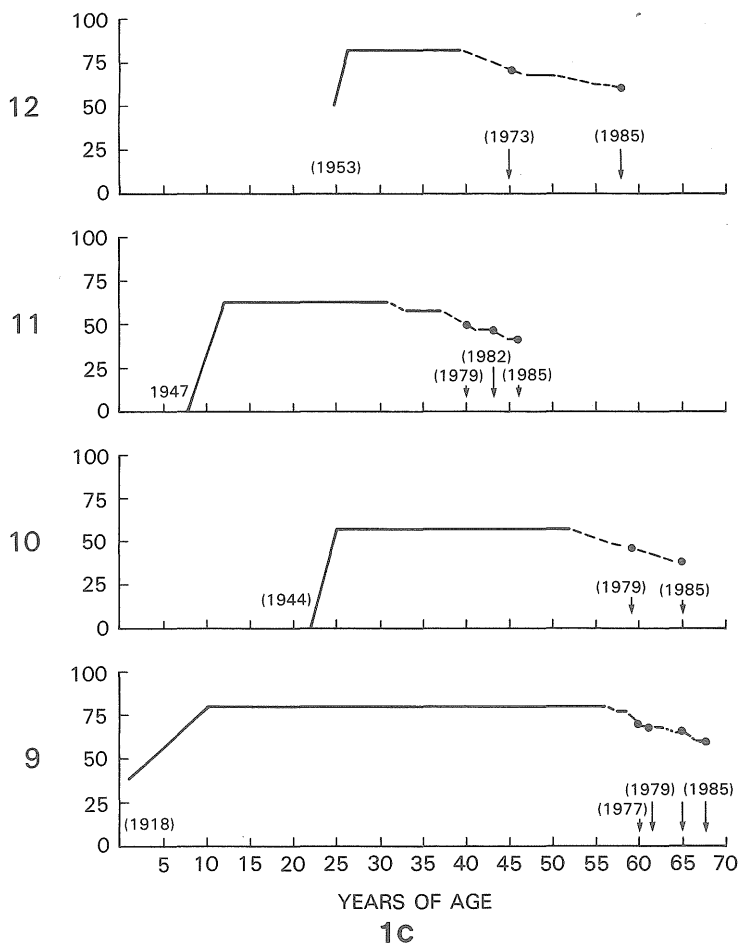


Fig. 1 (cont'd)

clinical description, old photographs, or medical records. None of the biopsied muscles had a known history of injury or needle insertions for at least 6 months prior to biopsy. Open muscle biopsy was performed according to standard techniques [11]. Specimens were fresh frozen in isopentane cooled to -160°C with liquid nitrogen. Ten micron sections of muscle were then processed for muscle enzyme histochemistry. Serial muscle biopsy sections were also stained with trichrome, acid phosphatase, and esterase to characterize the type of inflammatory cells. During the follow-up study, 8 post-polio patients who initially presented with new muscle weakness were rebiopsied to assess changes in the muscles during progression of the disease [12]. Thus, a total of 40 biopsies were analyzed.

Electromyographic (EMG) Studies

These included nerve conduction studies, routine needle electromyography, repetitive nerve stimulation studies, and single fiber EMG [7], using standard techniques [13]. These data were analyzed for fiber density, which is the average number of muscle fibers recorded by the needle during a single placement; jitter, which is the mean consecutive difference in the intervals between the activation of 2 muscle fibers in the same motor unit; blocking, which is the failure of a muscle fiber to activate when its motor unit is activated; and neurogenic jitter, which is the synchronous variation of at least 2 muscle fibers with respect to a third that must be due to an abnormality of the nerve rather than the neuromuscular junction.

Immunologic Studies

The serum and CSF from the patients with new muscle weakness and from 9 asymptomatic post-polio patients were tested for quantitative immunoglobulins by a nephelometric immunoprecipitation method and for oligoclonal bands using a high resolution agarose gel electrophoresis system [14, 15]. Search for circulating antibodies to neuronal or glial cells was performed by applying the serum to paraffin-embedded spinal cord sections using the indirect immunoperoxidase technique [16–18]. Peripheral lymphocyte subsets were analyzed in a flow cytofluorograph FC 200/4800 A (Ortho, Raritan, NJ) [19, 20] using the following monoclonal antibodies (Ortho) that identify surface membrane markers: OKT3 for T cells; OKT4 for helper/inducer T cells, OKT8 for suppressor/cytotoxic T cells, IgM for B cells, and OKIa₁ for B cells/monocytes/activated T cells. Immunochemical studies were also performed in these patients' muscle biopsies to look for deposits of immune complexes or immunoglobulins in the intramuscular blood vessels and nerves or in the muscle fibers by employing 5 μ fresh-frozen sections of muscles and fluorescein-conjugated goat anti-human IgG, IgA, IgM, C₃ and C₄ [16].

Virologic Studies

Search for antibodies to the polio virus was performed by the neutralization plaque assay and by ELISA in both the serum and the CSF of post-polio patients [21]. Titers of neutralizing antibody to poliovirus type 1 (Mahoney strain), type 2 (mouse embryo fibroblast strain), and type 3 (Saukett strain) were examined and the extent of the production of poliovirus antibody inside the blood-brain barrier was determined by making a correction for blood-brain barrier permeability using the ratio of CSF to serum albumin [22]. Both serum and CSF were also examined by ELISA for titers of antibody to measles virus (Edmonston strain) and to cytomegalovirus (CMV) [23, 24]. Antibodies to herpesvirus type 1 (McIntyre strain) and type 2 (multiple sclerosis strain), *Toxoplasma gondii*, and CMV (strain AD/69) were examined by indirect hemagglutination inhibition (IHA) technique [24].

Studies with Positron Emission Tomography (PET) Scan

The metabolic activity of the cortex in 3 post-polio patients with new weakness was examined with the PET scan and ^{18}F -2-deoxy-D-glucose [25] to see whether the viability and function of the upper motor neurons are affected when their lower motor neuron targets in the spinal cord are severely reduced, as occurs in the post-polio state. For this purpose, 3 post-polio patients with severe residual disability were selected.

Examination of the Spinal Cord

As reported elsewhere [26], the spinal cords from 8 post-polio patients who died from unrelated causes were examined histologically and the findings were correlated with the patient's residual deficit. We have specifically correlated changes in the spinal cord from post-polio patients with new symptoms as well as those without symptoms who died from 1 to 44 years after the original polio attack.

RESULTS

Clinical Observations

Excluding radiculopathies, compression neuropathies, back, knee or joint injuries, and osteoarthritis, the new neuromuscular symptoms in post-polio patients can be divided into 2 groups:

- 1) **Musculoskeletal symptoms.** In this symptom complex, we included patients with deterioration of functional capacity, with fatigue, joint pains, decreased endurance, and symptoms of "wear and tear," but not new weakness. These patients—after adjustment of their braces, involvement in new exercise programs, and physical therapy—usually improve and remain stable. We have found that anti-inflammatory agents such as ibuprofen (Motrin, Rufen) often substantially help these patients' functional abilities.
- 2) **Neurologic symptoms and signs: post-poliomyelitis progressive muscular atrophy (PPMA).** We have coined the term to describe new, slowly progressive muscle weakness, with or without muscle pains and atrophy, which occurs in certain muscle groups of post-polio patients.

Patients with PPMA, who usually have a milder residual deficit than the previous group with predominantly musculoskeletal symptoms, present with new muscle weakness and atrophy involving either the muscles that had been previously affected and had fully or partly recovered or muscles that were clinically unaffected by the original disease [5–8]. In all patients, the new weakness is asymmetric and often associated with increasing muscular atrophy. Some patients experience myalgias. Muscle pain in PPMA can be

disturbing but is very seldom severe. It is an intrinsic muscle pain, like the one we have described in neurogenic diseases [27], and not a joint pain, as described for the previous group. Some of the PPMA patients, however, may also have the musculoskeletal symptoms described above in addition to the new weakness, making a clear distinction difficult between the 2 groups. Occasional fasciculations are noted in all patients, even in muscles that do not appear to have become weaker, although in my view, fasciculations are more frequently seen in the newly weakened muscles.

The average period after the acute polio in which new symptoms develop is usually 30 to 35 years. Both males and females are probably affected with the same frequency, although in the first group with musculoskeletal symptoms, females are more frequent among the patients seeking medical advice. A typical course of a patient with PPMA is depicted in Figure 2.

Epidemiologic surveys showing the exact prevalence of PPMA, the sex distribution, and the frequency of the *musculoskeletal symptoms* or *PPMA* are not available at the moment. The data from mail surveys, without

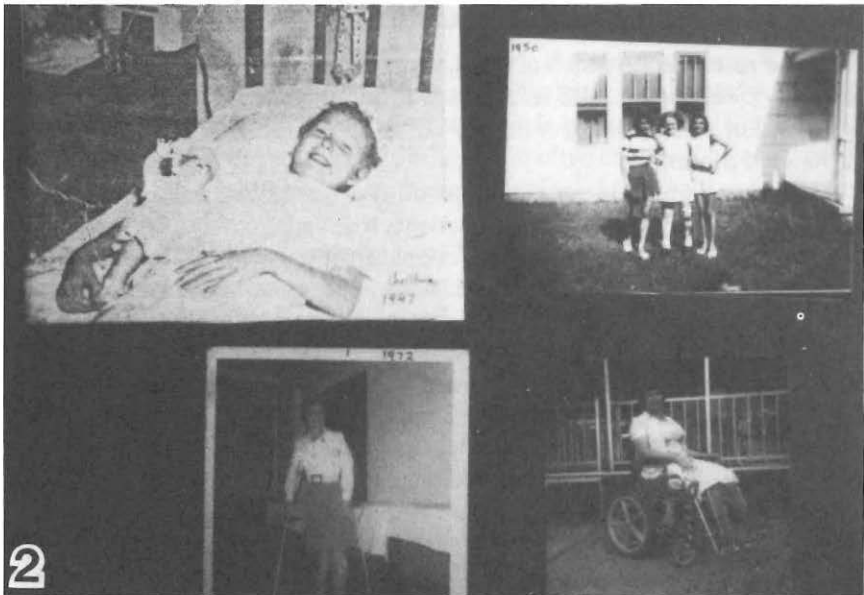


Fig. 2. Representative photographs of a patient with typical PPMA followed since the acute polio (1947) (top left) and subsequent recovery (1950) (top right). This patient, who was walking with only braces and crutches after full recovery, remained stable until 1972 (bottom left), when she started to experience new weakness in all her limbs necessitating return to a manual wheelchair a few years later. After further progression of the weakness in all her limbs, the manual wheelchair was replaced by an electric wheelchair (present time, bottom right).

examining the patients, are not accurate, as we discovered very early in our study when we mailed questionnaires to 2,500 post-polio victims (M.C. Dalakas, unpublished observations). Without examining the patient neurologically and asking specific questions, we found it very difficult to define which patients have musculoskeletal symptoms and which have PPMA. This distinction is important because prognosis and perhaps therapeutic approaches for each group are different. Furthermore, mail surveys cannot differentiate between other concomitant neurologic problems, such as radiculopathies, compression neuropathies, or other illness.

Another group of polio survivors, after hearing of the new post-polio problems and reading about them in the news, made a retrospective analysis of their neuromuscular performance and began believing that they may be having some of the symptoms described for PPMA. These patients are anxious and seek expert medical opinion out of fear of developing PPMA. They do not have PPMA but "pseudo-PPMA" and respond well to reassurance after a careful neurologic examination by a neurologist experienced in post-polio patients. Yearly follow-up visits are suggested for such patients.

Progression and Outcome of PPMA Patients

The rate of progression of PPMA, the future anticipated disability, and the risk of developing ALS as reported in some series [28, 29] has caused a great deal of anxiety and fear among the estimated 300,000 polio survivors in the United States.

In an attempt to answer some of these questions, we performed a follow-up study by reevaluating 27 patients who had recovered from polio and who were initially admitted to the National Institutes of Health from 1960 to 1981 because of PPMA. The diagnosis was made by complete neurologic and electrophysiologic examinations and studied by means of muscle biopsies and analyses of the spinal fluid. The availability of such well-studied patients, whose new weakness was clearly documented and quantitated based on the MRC rating scale, made such a follow-up study possible [7]. In addition, new changes in these patients' muscle biopsies and comparison with the previous biopsies were expected to provide insights into the mechanisms of PPMA.

When these PPMA patients were reexamined at the end of the follow-up period (average, 8.2 years; range, 4.5 to 20), their mean age was 50.5 years (range, 36 to 69); the mean age at which their new symptoms began was 39.6 (range, 25 to 56); and the mean number of years after acute polio when those symptoms began was 28.8 (range, 15 to 54); all patients were weaker and had a much lower level of function. The pace of worsening during the period between the first and last neurologic examination was very slow and varied from patient to patient and within individual patients. Some patients had a stepwise progression of weakness, with subsequent relative stability, whereas

others had a slow, continuous decline in strength. Figure 1 depicts the progression of weakness in the 12 patients who had the longest mean follow-up times in the study (11.6 years; range 6 to 20). In 4 of these patients (Nos. 5, 6, 8, and 9), the new muscle weakness had increased but remained almost completely confined to the same muscles that had appeared to be weaker during the initial examination; in 3 others (Nos. 1, 3, and 12), new weakness had appeared in additional muscle groups. Three patients (Nos. 7, 10, and 11), who had a more severe residual disability in one or more groups of muscles from the original disease, had increased weakness in all the other muscle groups. Although the new decline in strength was mild within each muscle group, the cumulative effect on the patients' overall neuromuscular function was considerable, and they had become severely disabled. In fact, all 3 were using electric wheelchairs, whereas 10 years earlier, they had required only crutches. The remaining 2 patients (Nos. 3 and 4), who were followed for 13 and 11 years, respectively, felt a very slight new generalized weakness, which did not substantially alter their life-styles or interfere with their everyday activities.

The mean total estimated loss of neuromuscular function for the 12 patients with the longest follow-up was 11.8 points (range, 7.5 to 17.5); for the other 15 patients (mean follow-up, 4.7 years), the mean loss was 4.1 points (range 2.2 to 6.5). However, the mean calculated total yearly loss was identical in both groups, ie, 1.05 points of muscle strength (range, 0.7 to 2.5). Generally, the new weakness was so mild that it often could not be appreciated on a year-to-year basis; the patients recognized weakness only over a longer period (mean, 3 years; range, 1 to 10).

None of the 27 patients had ALS, which is defined as new, rapidly progressive, generalized muscle weakness and wasting and the presence of upper motor neuron signs, bulbar signs, or respiratory difficulties. The age of onset of new symptoms, the sex of the patients, and the degree and type of physical activities of each patient before the manifestation of the new weakness were not factors in the progression of the weakness. All patients had remained active, with reasonable use of their unaffected limbs. From this follow-up study, it became clear that the degree of disability and final outcome of a PPMA patient depends on the neurologic status and degree of residual deficit each patient has at the "starting point" at which PPMA begins. Although PPMA is a benign condition and does not lead to ALS [7, 30], it can be serious only in those patients who at the "starting point" had a severe residual deficit. Thus, if post-polio patients who have been left with severe residual deficit of bulbar or respiratory muscles with minimal muscle reserves develop PPMA, the new weakness could affect the same, already very weak muscles, resulting in new bulbar symptoms and respiratory difficulties. This should not, however, be interpreted as ALS, as I have discussed

elsewhere [30]. The progression of the weakness in these muscles also is anticipated to take the same course as the one described for the limb muscles of PPMA (Fig. 1). In contrast, we have not seen any of our PPMA patients who, at their "starting point" had residual deficits confined only to the limbs, develop new bulbar or respiratory muscle weakness as part of the clinical picture and course of PPMA.

Blood Chemistries, Virologic, Immunologic, Biochemical, and Histologic Findings

Routine laboratory blood studies are normal in PPMA as in all the post-polio patients who do not have other concomitant illnesses. The only exception is the serum CK, which can be elevated up to fivefold in some PPMA patients. This does not necessarily indicate myopathy since CK can be elevated slightly in some neurogenic conditions such as ALS or spinal muscular atrophies. This is probably consistent with the "myopathic" changes we see in the muscle biopsies of some of the post-polio patients due to a chronic denervating state, as described below and elsewhere [12].

In reference to the virologic and immunologic investigations, PPMA patients had elevated antibodies to the polio virus in the serum [5, 6, 8], as expected, since they had been infected with the polio virus. There was no specific elevation of the polio virus antibodies in the CSF to suggest reactivation of the original polio virus when we calculated the ratio of the polio antibody titers in the serum and CSF [5]. Search for antibodies to the other viruses was also negative. The lymphocyte subsets, described earlier as abnormal in some of the early PPMA patients we studied [5, 6], have not been consistently abnormal in the follow-up investigation of the same and other patients. But even in our original patients, these lymphocyte subsets were internally inconsistent in providing specific immunologic or clinical information. These findings are of uncertain significance. Immunocytochemistry on the muscle biopsy specimens was negative for immune deposits of immunoglobulins and complement. Similarly, antibodies to neuronal components could not be found immunocytochemically when the patient's serum was applied to sections of spinal cord.

The most interesting observation in our immunologic investigations was the presence of IgG oligoclonal bands in up to 50% of PPMA patients but not in the 9 post-polio controls that we studied, even early after the acute viral illness (Dalakas et al, unpublished data). The significance of these bands is now under study to investigate whether they represent antibodies to the polio virus or to other neuronal components. We did not find specific CSF IgG synthesis for the polio virus, based on our calculations of the polio virus antibodies in the serum and CSF after correction for blood-brain-barrier permeability [5, 6].

The PET scan studies revealed a normal cortical metabolism in PPMA patients, which clearly indicates that the upper motor neurons, if deprived of their lower motor neuron targets, continue to maintain normal cell function. The integrity and function of the upper motor neurons therefore does not depend on a signal from its lower motor neuron target via the corticospinal tract. This is in contrast to the spinal cord lower motor neurons that appear to degenerate when their target is lost after axonotmesis [31]. The normal PET scan in PPMA reinforces the differences between PPMA and ALS, where there is an average of 22% reduction in the regional cerebral metabolic rate for glucose throughout the cortex and basal ganglia [25].

The examination of the spinal cords from the old post-polio patients and those with PPMA provided new insights into the pathogenesis of the post-polio new weakness. As we report in this volume [26], the most striking finding in the post-polio state was the presence of perivascular and interparenchymal inflammation in post-polio patients' gray matter, regardless of whether they had stable post-polio or PPMA. In addition, active gliosis, neuronal chromatolysis, and axonal spheroids were noted. All these findings suggest a continuous neuronal activity that, although subsided, has not ceased after the original viral attack.

Laboratory Investigations for the Diagnosis of PPMA

To understand the mechanism of PPMA, there are 2 additional investigational tests, the EMG and the muscle biopsy. In addition to helping us understand the disease, these tests could be of specific diagnostic value. These 2 procedures do not need a sophisticated laboratory, but only a careful interpreter, and they are available everywhere, even in community hospitals.

Electromyography. Our electroneurographic studies were performed in several stable post-polio and all the PPMA patients. In those PPMA patients included in our follow-up studies, EMG was done twice during the initial and follow-up investigations [7, 32]. Electroneurographic studies revealed normal motor and sensory conduction velocities and action-potential amplitudes. Repetitive-stimulation studies of the ulnar nerve and (occasionally) of the axillary nerve showed no pathologic decrement at 4 Hz and no pathologic increment at 50 Hz. EMG studies showed widespread chronic denervation with large-amplitude voluntary motor units (up to 25 mV) in almost all muscles studied. Chronic denervation was observed even in muscles that were apparently not involved in the original attack of polio. Fibrillation and positive sharp waves were seen in sparse-to-moderate amounts in many muscles, but the presence of these findings did not correlate in an obvious fashion with the recent deterioration. Fasciculations were seen in most of the patients, but the discharge frequency was very low ($<1/\text{min}$). Fasciculations appeared to be more frequent in the weakening PPMA muscles.

The single-fiber EMG studies carried out in some patients showed an increase in fiber density and many fiber clusters (groups of 3 or more fibers with small time differences that made formal jitter analysis impossible). Increased jitter and blocking were seen in most muscles, and the amount of jitter and blocking appeared to correlate with the degree of recent deterioration. Neurogenic jitter was not observed. These findings confirm previous electrophysiologic studies [33].

The prevalence of spontaneous activity and abnormal jitter indicates an ongoing process of remodeling of the motor units from denervation and reinnervation. It appears that this process occurs diffusely in all post-polio muscles independent of power, clinical stability, or age [32]. The EMG in the clinical diagnosis of PPMA is therefore helpful only to rule out other concomitant neuromuscular disorders (neuropathy, myopathy, radiculopathy, etc). Unfortunately, it does not differentiate PPMA from stable post-polio state. The differences and similarities in the EMG findings between PPMA and ALS are described elsewhere in this book [30].

Muscle biopsy. Muscle biopsy studies of previously recovered and newly affected muscles (performed twice in 8 patients, during the initial and follow-up visits) confirmed the presence of reinnervation, which was indicated by the formation of large groups that contained both type I and type II fibers (Fig 3). These groups were very large, containing up to 170 fibers per group,

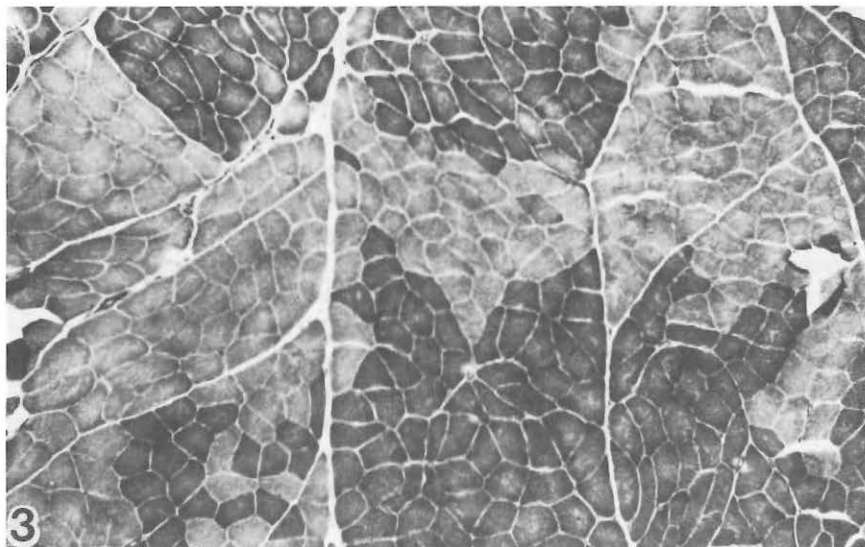


Fig. 3. Muscle biopsy from a fully recovered post-polio muscle shows very large groups of both type I and type II muscle fibers indicative of substantial reinnervation.

and appeared to be present in different sizes in all the post-polio muscles regardless of new weakness, suggesting that polio was a generalized disease of the spinal cord motor neurons. Although grouping was present in all the biopsies, regardless of new symptoms, the most characteristic finding in only the newly weakened PPMA muscles was several isolated, atrophic, angulated

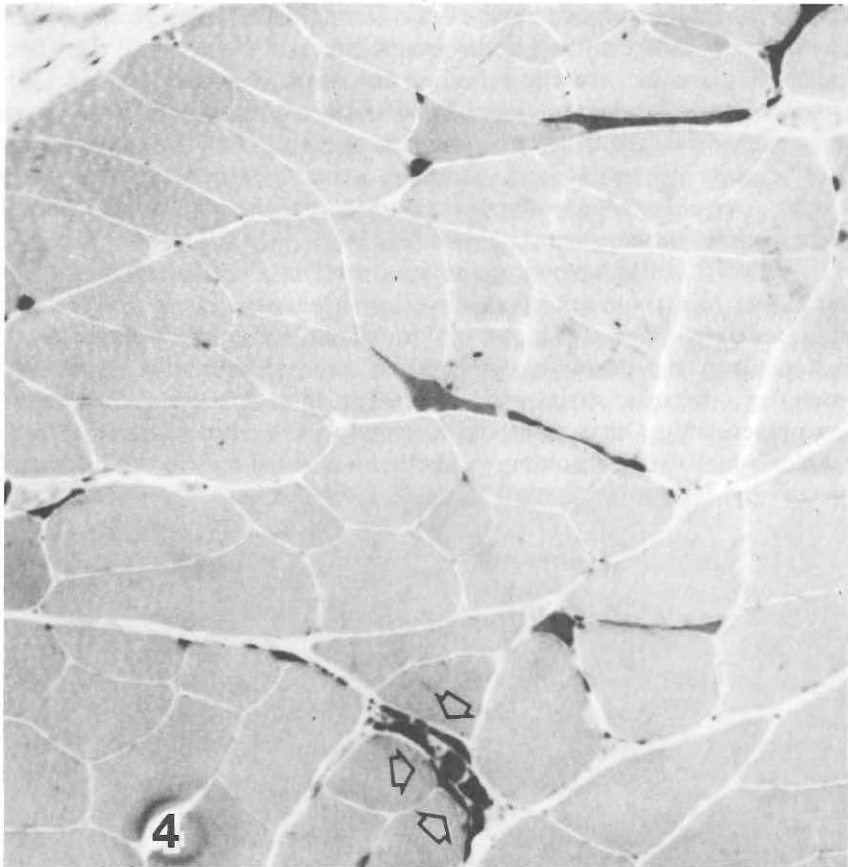


Fig. 4. Transverse frozen section of a muscle biopsy specimen stained with nonspecific esterase, from a PPMA patient. Note the scattered, small, angulated fibers with the dark stain. The same type of change, but to a milder degree, was noted in the same muscle of the same patient during a biopsy examination 12 years earlier, when the muscle was slightly stronger. Although no groups of atrophic fibers (indicative of loss of the whole motor unit) were noted in most of the patients, occasional small group atrophy can be seen as in this biopsy specimen (arrows). This can conceivably happen with further progression in PPMA muscle when some adjacent atrophic fibers form a small group due to loss of axonal sprouts that belong to the same or neighboring motor neurons.

fibers compressed in the interstices between large fibers (Fig. 4). These small fibers, which stained darkly with an enzymatic reaction, are characteristic of new active denervation. The fibers remained isolated and scattered randomly, even throughout the follow-up period. No clusters of atrophic fibers (group atrophy) were observed, even in the muscles subjected to 2 biopsy evaluations. This is in contrast to the findings in the weakening muscles of patients with ALS, in which the atrophic fibers always form groups (group atrophy), and the number of atrophic fibers in the groups increases rapidly until the whole fascicle is atrophied, thereby reflecting the death of whole neurons [30]. Although typical group atrophy was not found, several atrophic fibers were sometimes adjacent (Fig. 4). This suggests that as PPMA progresses, some more adjacent fibers will become atrophic, eventually producing small group atrophy as more distal axonal sprouts that belong to the same or neighboring motor neurons continue to disintegrate [12, 34].

In 12 of 27 PPMA biopsy specimens (including those from muscles that had 2 assessments), occasional small perimysial or perivascular lymphocytic infiltrates were observed (Fig. 5), confirming our earlier observations [5–8]. In 2 patients, the degree of lymphocytic response was more prominent, prompting a therapeutic trial with 100 mg of prednisone; however, the therapy was unsuccessful. Other morphologic features were also noted in PPMA muscles, which varied according to whether a biopsied muscle was originally affected and had fully or partially recovered. As previously described [12], in

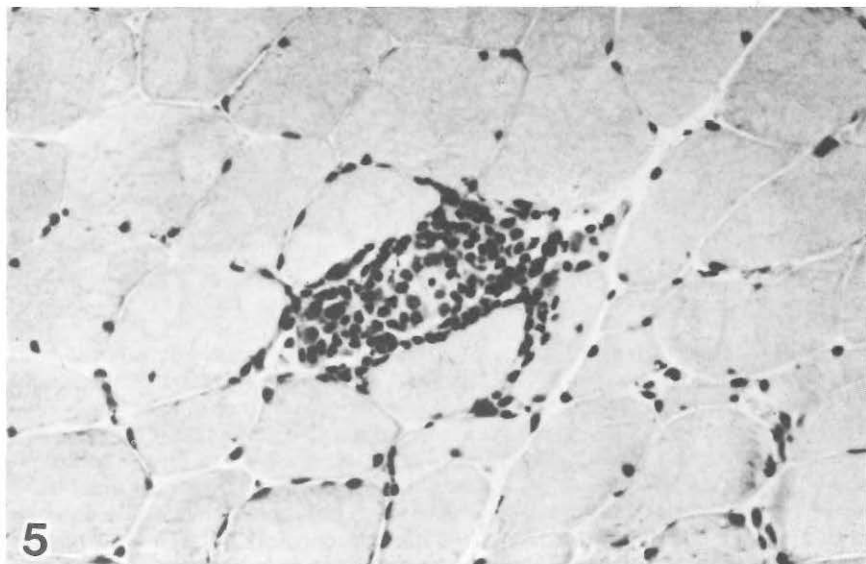


Fig. 5. Muscle biopsy from a PPMA patient reveals perivascular inflammatory infiltrates consisting of lymphocytes.

partially recovered muscles, there was a mixture of chronic neurogenic and myopathic findings similar to those described in muscles undergoing chronic denervation (Fig. 6). In previously affected but fully recovered—and now newly symptomatic muscles—hypertrophic fibers with splitting, internal nuclei (Fig. 7) and targetoid or moth-eaten fibers were prominent [12]. Clearly these findings are not present in ALS muscle biopsies [12, 30].

DISCUSSION

Among the spectrum of the new neuromuscular symptoms that post-polio patients develop, those that appear to be specifically related to the dysfunction of the remaining motor neurons fall within a specific clinical description that we call PPMA. The other symptoms that post-polio patients often experience are *musculoskeletal* in nature and appear to be amenable to therapeutic interventions with anti-inflammatory agents or physical therapy. The clinician should be able to differentiate between the 2 except in those cases when both groups of symptoms coincide. Other symptoms resulting from long-term disability, especially due to wheelchair confinement, such as compression neuropathies, radiculopathies, degenerative arthritis, depression, obesity, or gastrointestinal dysfunctions, should be sought and ruled out before the

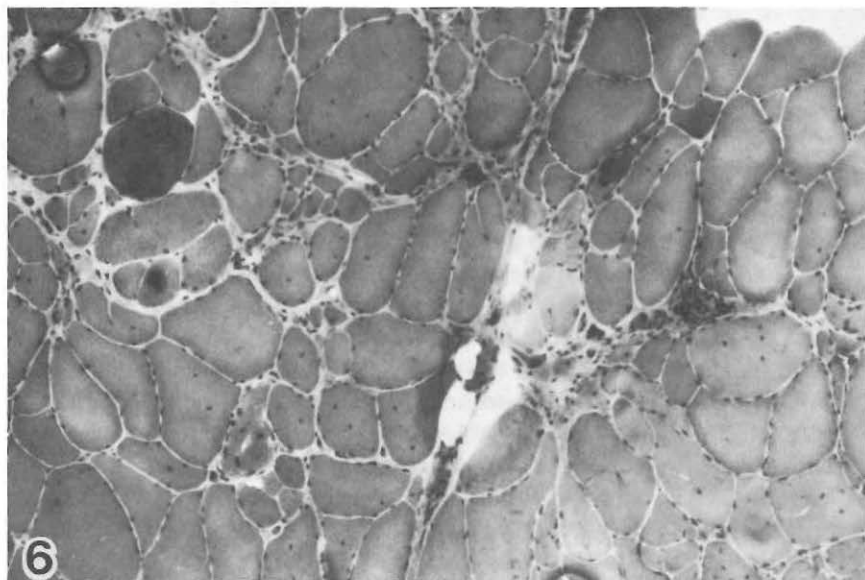


Fig. 6. Muscle biopsy from a PPMA muscle that was originally affected and partially recovered. Note typical features of myopathy with variation of fiber size, increased connective tissue, internal nuclei, and necrotic fibers. (Myopathic features due to long-standing denervation.)

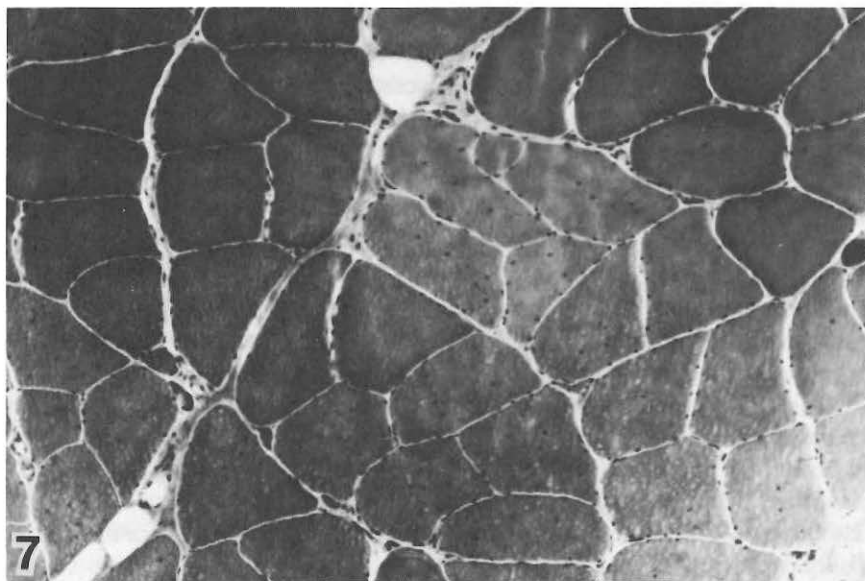


Fig. 7. Muscle biopsy from a PPMA patient taken from a previously affected and fully recovered muscle. Note large size fibers with splitting and internal nuclei (work hypertrophy?)

diagnosis of PPMA is considered. These symptoms, which appear to result from the chronic disability of post-polio patients, may not be different or less frequent from the symptoms of other non-polio disabled patients that use wheelchairs or crutches, such as victims of spinal cord injuries, cerebral palsy, or stroke. For these reasons, I strongly object to their being included within the "post-polio syndrome" description, which should include only symptoms characteristic of the post-polio state. Because these symptoms are sometimes the most prominent in the patient's clinical picture and other times overlap with the symptoms of PPMA, it is our responsibility to diagnose and treat or comfort the patient and guide him/her to the appropriate therapist.

PPMA is a specific clinical entity. It is not a life-threatening neuromuscular condition unless the new weakness begins in a post-polio patient who already has a very advanced disabled condition with minimal respiratory muscle reserves from the original polio attack. Our follow-up study of patients with PPMA after a mean period of 8.2 years from the time we had first seen them at the National Institutes of Health showed that the muscular weakness in PPMA is progressive. However, the degree of decline of the neuromuscular function is slow, predominantly focal, and minimal (Fig. 1). We estimated the rate of progression as one point of the total 100 points of muscle strength per year [7], but we stressed that progression varies from patient to patient and

within individual patients, who often have long periods of subjective stability. In fact, new weakness is not often objectively appreciable on a year-to-year basis but only over cumulative periods of 3 years [7]. The overall progression, although minimal, has a substantial effect on neuromuscular function in patients in whom polio had caused severe disability and limited muscle reserves, ie, patients who at best were functioning at or below 50% of their total strength. Contrary to previous reports that ALS or an ALS-like disorder occurs more frequently in persons who have had polio, none of the 27 patients in our follow-up study, who were followed for a mean of 8.2 years (range, 4.5 to 20) from the time they were originally examined and up to 12.2 years (range, 6 to 29) from the onset of their new weakness, were found to have ALS, as indicated by generalized muscle weakness and wasting and respiratory, bulbar, or upper motor neuron signs. Similarly, none of a recent group of 25 persons who had recovered from polio and who had been referred to the National Institutes of Health because of new weakness had ALS (M.C. Dalakas, unpublished data).

PPMA is not only a clinical diagnosis. If in doubt, it can be substantiated by muscle biopsy of a newly weakened muscle showing recent denervation in the form of small scattered angulated fibers [12], which we consider a specific finding for PPMA. The EMG should be done, and it is helpful to exclude other conditions, but it is not specific for PPMA, because signs of denervation can be equally present in weak and strong muscles and in stable or newly weakened muscles.

PPMA appears to be a disorder of the motor neuron, and its pathophysiologic aspects differ in a number of ways from those of ALS, the archetypal disorder of motor neurons [7, 30]. Clinically, PPMA is predominantly focal and always progresses slowly, without producing upper motor neuron signs or involvement of bulbar muscles except when there is a preexisting weakness of those muscles from the original polio. In biopsy specimens of newly weakened muscles of patients with PPMA, the denervation is characterized by a few single, scattered, angulated fibers and by large fiber-type grouping, rather than by the atrophic muscle fibers that form in groups (group atrophy) because of the death of the whole motor neuron that are typically seen in the weakened muscles of patients with ALS. This observation on the type of denervation was reinforced by follow-up muscle biopsies in 8 of our patients, which indicated that even though the patients had a mild but progressive weakness for a mean of 11.6 years, the weak muscles showed signs of very small group atrophy only on very rare occasions [7, 12, 32].

ALS is caused by the death of anterior horn cells. In contrast, it would be reasonable to assume that PPMA is caused by the death of individual nerve terminals in the motor units that remain after polio, rather than the death of the whole unit. This would explain most of the clinical, physiologic, and

histochemical features of the syndrome. As each terminal dies, the weakness progresses slowly. Regeneration proceeds muscle fiber by muscle fiber, and there is no opportunity to form new groups of fibers. This theory is supported by the presence of single, scattered, angulated fibers in the muscle biopsy specimens (without group atrophy) and the observation by means of single-fiber EMG that there is no "neurogenic jitter." In single-fiber EMG, increased jitter can be due to instability at the neuromuscular junction or at the branch points of axons. Newly regenerated axons may show instability at the points of the axon branches during active reinnervation. Neurogenic jitter, which is characterized by groups of action potentials that jitter together, can be seen in patients with ALS. Its absence in our patients with PPMA supports the observation that there is a lack of reinnervation of groups. Although no group atrophy was noted in the newly weakened muscles, I should emphasize that as PPMA progresses, some adjacent fibers can become atrophic (Fig. 4), and eventually, a small group atrophy can develop as more distal sprouts that belong to the same neighboring motor neurons continue to disintegrate [34].

Deterioration of individual nerve terminals in PPMA might be an outcome of the process of recovery from an acute attack of polio. After such an attack, the surviving motor neurons sprout to reinnervate more muscle fibers than normal. This process produces large motor units that may stress the cell body. After a number of years, these hyperfunctioning motor neurons (with their excessive sprouting) may not be able to maintain the metabolic demands of all their sprouts, and a slow deterioration of the individual terminals may result [7, 34]. Some individual fibers may be able to be reinnervated a second time, but eventually enough nerve terminals are destroyed and enough reserves are diminished for weakness to appear. After acute polio, there is always reinnervation [7, 12, 32, 34] but in PPMA, the reinnervation in the newly weakened muscles has reached such overwhelming proportions that failure of further reinnervation is inevitable. This would be consistent with the focal nature of PPMA and its very slow, stepwise, unpredictable progression. Normal aging alone cannot be responsible for this process, since neuronal loss does not occur in persons younger than 60, and muscle biopsy specimens from normal persons who are younger than 70 rarely show small, scattered, angulated fibers [35].

PPMA appears to be clinically manifested approximately 30 years after the original polio attack, which suggests that the remaining post-polio neurons that have been overfunctioning to maintain very large motor units have a shorter life-span. From our studies, 2 additional interesting observations also emerged that could enlighten our understanding of the neurobiology of motor neurons. First, it appears that the previously damaged but survived motor neurons continue to demonstrate signs of instability at the level of their distal axon terminals, as supported by the presence of fibrillations (and occasionally

fasciculations) even in the stable muscles. This is clearly different from a static nerve injury in which after reinnervation, electrophysiologic stability is complete within a period of 12 to 18 months. The reasons that the motor neurons continue to remain unstable may reflect an inherent property (perhaps via peripheral stimulation) to constantly compensate for their disintegration of axonal sprouts.

Our second observation complements the electrophysiologic instability of post-polio motor neurons. In the spinal cord of even neurologically stable post-polio patients, we have noticed active inflammation, gliosis, neuronal chromatolysis, and axonal spheroids from 1 to 44 years after the original polio attack. These findings suggest that although the viral attack on the motor neurons took its original toll of a number of neurons and poliomyelitis is a monophasic disease, some residual "sparks" have remained in the surviving neurons that appear to cause an indolent but continuous inflammation leading to a subclinical neuronal dysfunction. Whether these "sparks" represent residual viral genomes and PPMA is a slow viral illness remains to be determined. Such a hypothesis could provide an explanation for the oligoclonal CSF IgG bands that we have noted in some PPMA patients. Alternatively, the inflammation in the spinal cord could represent a response to a continuous mechanical, indolent injury via retrograde flow as the result of the dying axonal sprouts.

The electrophysiologic instability of clinically "stable" post-polio muscles along with the histologic signs of inflammation and neuronal chromatolysis in the stable post-polio state suggest that PPMA is the end of the spectrum of an ongoing neuronal reaction that has not completely ceased after the acute viral insult but continues many years later, slowly affecting the ability of the surviving neurons to maintain the integrity of their distal nerve terminals and their capacity for additional axonal sprouting. The clinical manifestation of new weakness in PPMA could therefore represent the "tip of the iceberg" in such continuously dysfunctioning neurons; when enough reserves have diminished, more nerve terminals cannot survive, and further reinnervation cannot take place.

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DISCUSSION

DR. DAUBE: In making the comparison between those patients who are progressing or those limbs that are progressing and those that are not, I think that it is essential that there be matching of the severity of the involvement of the muscle. In your biopsies or in your electrophysiologic studies, did you match so that the muscle that was asymptomatic, not progressing, was in fact equally severely involved?

DR. DALAKAS: No, we did not. You indicate an ideal situation for the post-polio study, but I do not know if this is practically feasible or it would be possible to do in a large number of patients.

DR. MUNSAT: You have demonstrated so nicely inflammatory changes in muscle, globulin abnormalities in spinal fluid, inflammatory changes around the anterior horn cell at time of autopsy, and the electrophysiologic findings that we have heard of instability and reorganization of motor units. Most of the talk has been in terms of pathogenesis but, based on these observations, do you feel that these findings would be caused by the normal age-related alterations in the alpha motor neuron or is it more likely that a virologic/immunologic process is still active?

DR. DALAKAS: You raise 2 very important questions. The aging process, as we know from the elegant studies of Professor Tomlinson, starts in the neurons

after the age of 60. For these reasons specifically, we elected to study patients who were below the age of 60. In the muscle biopsies that we did in a previous study, looking at the muscle changes in normal aging people, we found some angulated fibers and mild fiber type grouping in normal people above the age of 70. So, in our selected patients, the findings I described are not due to aging, per se.

In reference to your second point, I really do not know why we have inflammation in the muscle, inflammation in the spinal cord, and ongoing EMG changes. We can hypothesize and speculate about several possibilities as I discussed, but I cannot really answer the question if these changes represent secondary phenomena or if there is indeed an ongoing viral activity.

DR. McCOMAS: In relation to Dr. Munsat's question about aging, it is true that whole motor units seem to lose function after the age of 60. This was Tomlinson's work and also the results of our motor unit counting work. However, if you measure muscle strength as we recently published in the *Journal of Applied Physiology*, it seems quite clear that in the ankle dorsiflexors and plantar flexors, strength starts to fall off in the early 50s. So it may well be as you implied that there is a stage where individual nerve twigs stop functioning and that this happens perhaps some years before the rest of the motor units degenerate.

DR. PERRY: I would like to make a comment on the effects of aging on strength. We have looked at a group of normal elderly people, average age 70. We have looked at 3 muscle groups: hip extensors, quadriceps, and hip abductors. What we have found is about a 50% loss in hip extensors and quadriceps strength as compared to a normal group of average people. But, we found no loss in the hip abductors. This suggests to me that a lot of our recorded strength loss is decreased activity, and the faster you go, the more you use your quadriceps, in other words, the more you use your extensor system in this sagittal plane. But, you still only lift your body away from the abductors and so that load has not changed. Just one more comment on aging. Comparing muscle changes between quadriceps and biceps, in the 70 and around 80 year olds, so-called clinically healthy men and women, there are quite a lot of differences, with less reduction in size of muscle fibers, especially type II fibers, in the upper limb than in the lower limb, indicating differences in activity pattern affecting strength.

Muscle Morphology With Special Reference to Muscle Strength in Post-Polio Subjects*

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INTRODUCTION

It is now well documented that polio survivors may experience an onset of new muscular problems around 30 to 40 years after acute polio [1]. There is definitely a need to better understand the causes of such a sudden reduction in muscle function. The epidemiology of these changes is difficult, and no acceptable study from the epidemiologic point of view has yet been conducted. There are quite a number of hypotheses concerning the possible causes of the muscle changes. It has been suggested [2] that many of the surviving motor neurons carry permanent scars from the polio virus infection and are just not able to keep pace with the metabolic demands of innervating all their muscle fibers. Another cause of this late-onset weakness could be an effect of natural loss of the neurons with aging; the subsequent loss of a few motor units with a normal aging process can have a significant effect on individual muscle strength. However, in normal subjects there may not be any significant loss of motor neurons before the age of 60, as demonstrated in studies of the human lumbosacral cord [3]. This process could therefore hardly explain the loss of muscle function below that age in post-polio subjects. There is definitely a need for further knowledge of the muscle structure of post-polio subjects and its adaptability to muscle activity. This report emphasizes measurement of muscle strength and its relation to muscle morphology. Are there special changes in the muscle structure and functions that could explain the change in function? This study will be followed by a report on a training study and studies on single-fiber electromyography.

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METHODS

Subjects

The present subjects were selected from a larger group of post-polio patients studied in Göteborg. The selection criteria for the whole group were that they had had their polio at least 25 years ago and were 40 to 65 years of age. For the present substudy, the subjects had to have maintained at least muscle strength, to perform a full knee extension in the sitting position. Muscle strength was measured in 13 men (42 to 61 years of age) and 17 women (41 to 65 years of age). Of these subjects, 9 men (44 to 61 years of age) and 10 women (41 to 65 years of age) volunteered for the muscle biopsy study. These 19 subjects had had acute polio 25 to 34 years ago. All measurements were performed on the same day. Informed consent was given by all subjects and the procedure was approved by the Ethical Committee of the Faculty of Medicine, Gothenburg University, Sweden.

Muscle Strength Measurements

Muscle strength was measured using a modified Cybex II muscle dynamometer with a specially designed computer program, including compensation for the torque due to the weight of the lower leg and the lever arm of the dynamometer [4]. In this presentation, only values from the weakest side are given. Isometric muscle strength was measured at a knee extension of 30° and 60°, and isokinetic strength during knee extension with angular speeds of 30°, 60°, 180°, and 300°/second. Three curves were recorded and the highest peak torque values are reported.

Muscle Biopsy

Muscle biopsies were taken from the middle portion of the right vastus lateralis (halfway between the upper border of the patella and the anterior iliac spine) under local anesthesia with an alligator forceps. The muscle specimens were divided into 2 parts: one part was frozen immediately in liquid nitrogen and used for analysis of enzymatic activities, the other part was trimmed, mounted, and frozen in cooled isopentane and used for histochemical analysis. Both parts were stored at -80°C until analyzed. For histochemical analysis, serial transverse sections (10 μ m) were cut with a cryotome at -21°C. The myofibrillar ATPase method was used for muscle fiber classification. The reactions were carried out at pH 9.4 following alkaline preincubation (pH 10.3) to classify fibers into type I and type II fibers. The type II fibers were subclassified into IIA and IIB fibers using preincubation at pH 4.6 and 4.3.

Measurements of the fiber areas were made on photos of NADH activity, stained, transverse sections. An optical illumination device ("particle size

analyses," Carl Zeiss, Oberkochen, West Germany), projecting the muscle fibers as circles of varying size, was used and the total fiber area was approximated. Measurements were made on 395 ± 38 fibers.

For the histopathologic evaluation, hematoxylin-eosine and modified Gomori-trichrome staining were also used as well as periodic-acid Schiff (PAS) reaction for glycogen. Group atrophy was defined as groups of 3 or more adjacent fibers in the field using light microscopy. A large grouping was defined as more than 16 fibers of the same type grouped together.

For biochemical assays, the enzyme activity was determined by means of fluorimetric techniques using a Farrand ratio-fluorimeter-2 (Farrand Optical Co., NY). The reactions catalyzed by the enzymes under investigation were coupled to NAD-NADH-linked reactions and determined according to the principles given by Lowry and Passoneau [5]. Analyses were made of triphosphate dehydrogenase (TPDH), lactate dehydrogenase (LDH), myokinase (MK), and citrate synthase (CS). The assays were performed at 37°C. The protein content was determined in order to express the activities per gram of protein.

Statistics

For statistical analysis, Wilcoxon's nonparametric test was used for differences between groups; for analyses of correlation, Spearman's rank correlation test was used.

RESULTS

As can be seen in Figure 1, the polio subjects had markedly reduced muscle strength compared with 2 control groups studied in our laboratory, one from middle-aged healthy men and women (unpublished material) and one from studies on systematically selected 70-year-old men and women in Göteborg [6].

In 9 of the 19 subjects studied with muscle biopsy, more than 70% (range 70% to 100%) type I fibers were seen. The rest of the subjects had 9% to 42%. Thus, the fiber distribution was separated into two groups (Fig. 2). The subjects usually had somewhat more type IIA than type IIB fibers, but in some subjects, as a result of the high proportion of type I fibers, few or even no type II fibers were recorded. Type IIC fibers were seen in low numbers in some of the subjects.

There was a negative significant correlation ($P < 0.05$) between muscle strength and the percentage of type I fibers using both isometric and isokinetic strength values. An example of this correlation is seen in Figure 3.

Large cross-sectional areas of the muscle fibers were found in a number

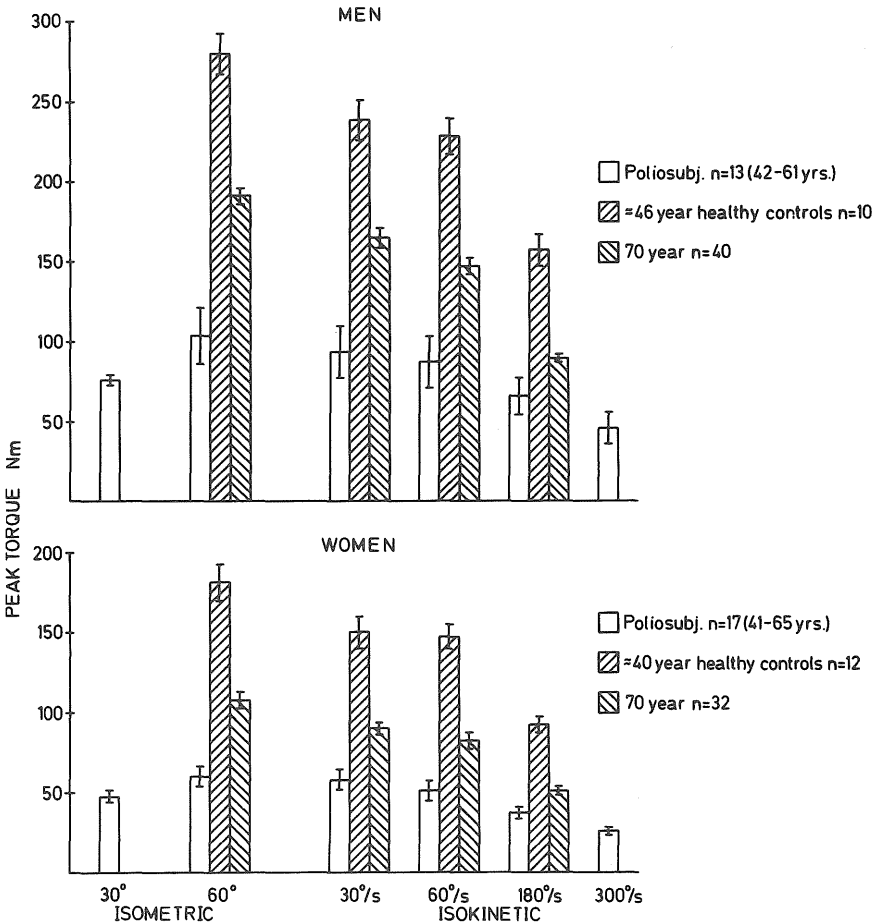


Fig. 1. Maximal torque during isometric knee extension with knee angle of 30° and 60° and peak torques during isokinetic knee extension with angular velocities 30° to 300°/s in post-polio subjects, healthy control groups studied in our laboratory (in their 40s, unpublished material) and 70 years of age [6]. Mean values and standard error of the mean are given.

of subjects, most of them with a large number of type I fibers. There was a large individual variation, as seen in Figure 4. As expected, the fiber areas in women were lower than in men, especially for type IIA fibers, and less so for type I fibers. On the average, the fiber area values were high, with a mean fiber area in the order of $8 \mu\text{m}^2 \times 10^3$.

Correlation analyses showed a negative significant correlation between muscle strength and fiber areas, as exemplified in Figure 5, with the

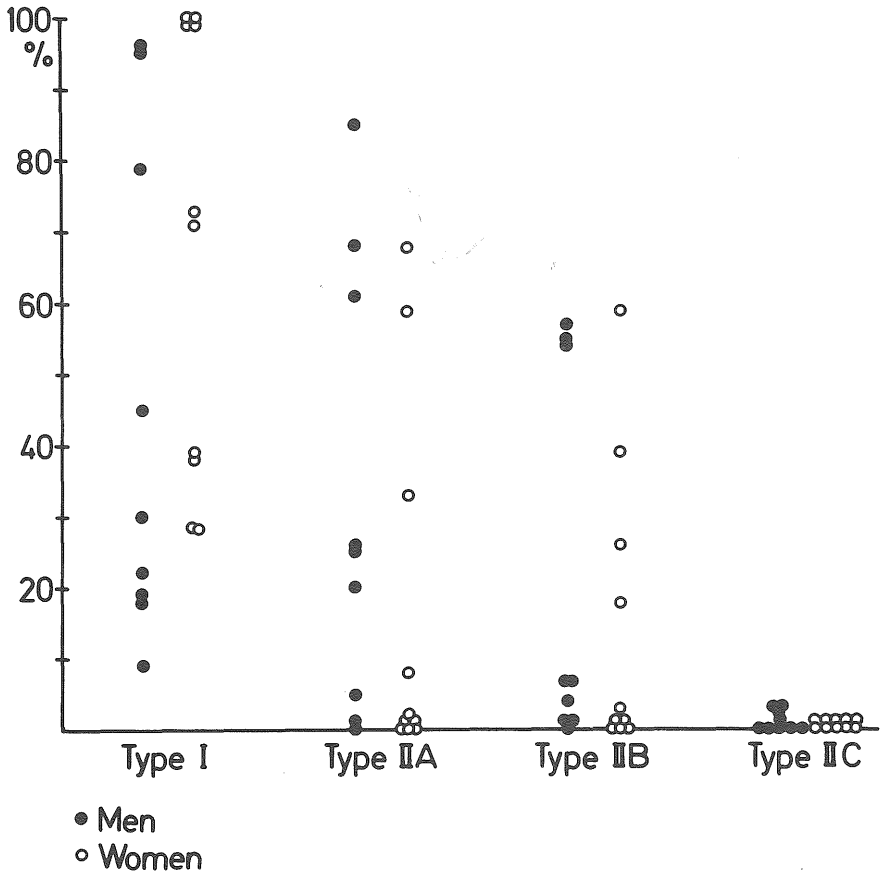


Fig. 2. Fiber distribution in muscle biopsy from vastus lateralis in male and female post-polio subjects.

correlation between muscle strength measured isokinetically at 30°/second and the mean fiber area in men ($P < 0.001$). However, these correlations were found only in men.

The histopathologic findings in the 19 studied subjects are summarized in Table 1. Grouping of one fiber type (>16 fibers) was seen in most of the subjects and for both fiber types. Most subjects had atrophic fibers, but they were grouped in only a few of the subjects. Although internal nuclei were common in more than 3% of the fibers, they comprised more than 10% of fibers in only a few subjects. Splitting in a few fibers was seen in around half of the subjects.

The activity of citrate synthase was low even when compared with our

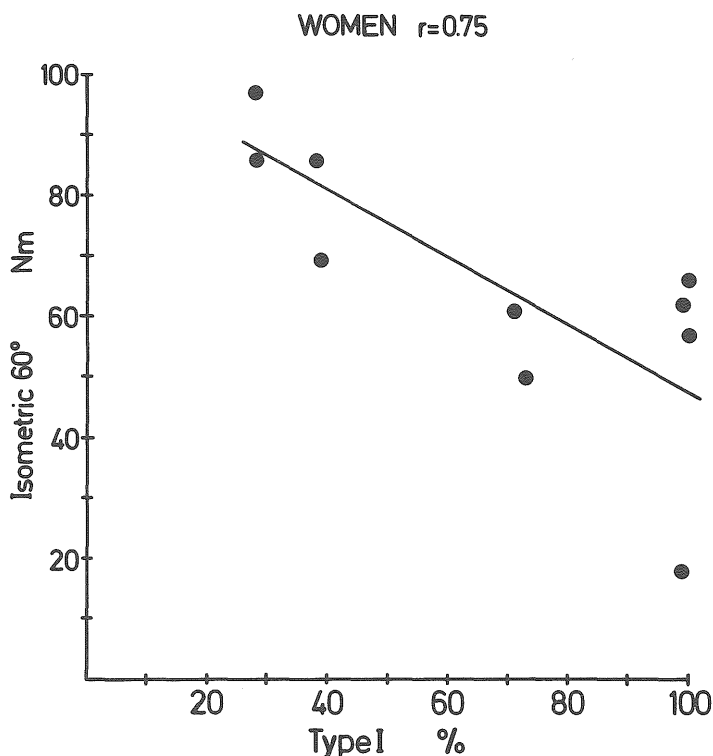


Fig. 3. Relationship between isometric knee extension strength measured at 60° knee angle and the relative occurrence of type I fibers in female post-polio subjects.

controls of clinically healthy 73- to 83-year-old men studied using an identical technique [7]. The activity of the other enzymes studied was more in the range of the control group of elderly men, but with a large individual variation.

DISCUSSION

The reduced muscle strength corresponds with the general reduction in muscle mass and muscle strength seen in the post-polio condition and also studied in other muscle groups using manual muscle testing. The quadriceps muscle was chosen for this particular study as muscle biopsies were included and could easily be taken in the vastus lateralis muscles. The strength values should therefore only be considered as examples of the reduction in muscle strength that could be seen in post-polio subjects. It should be noted that strength values were only measured in those who could perform a full knee extension. There is a reduction in strength with increasing angular velocity, as

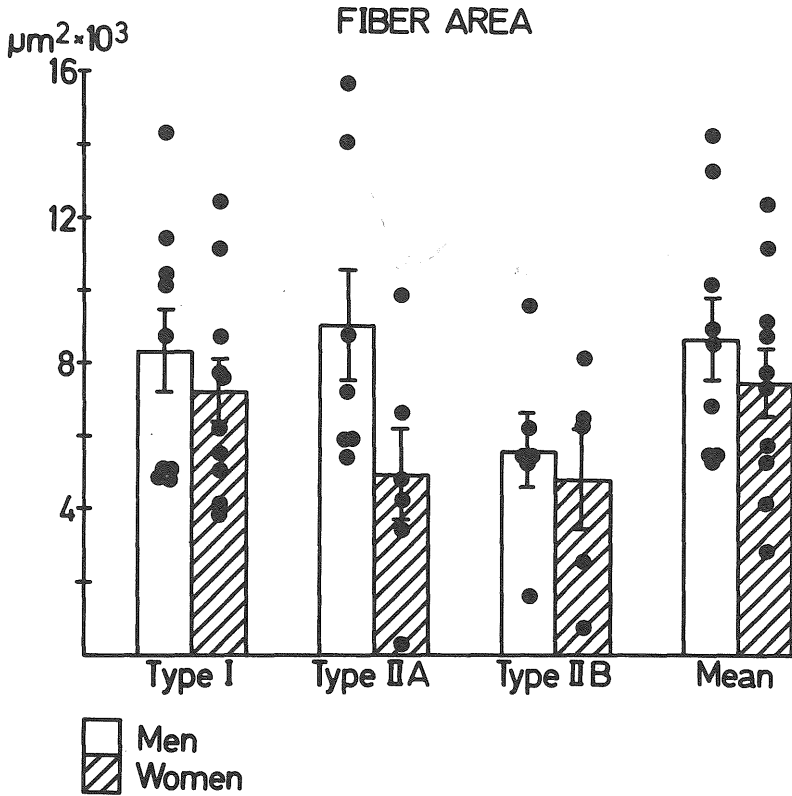


Fig. 4. Fiber area for various fiber types and mean fiber area in muscle biopsies from the vastus lateralis in male and female post-polio subjects. Mean values and standard error of the mean are given.

seen in healthy subjects, and the highest torque values were recorded with isometric measurements at 60° knee angles.

An interesting finding in the study is the high proportion of type I fibers found in half of the studied subjects. In fact, in 2 women, only type I fibers were noted. This is in sharp contrast to the normal finding in the vastus lateralis muscles, where there is usually an equal proportion between type I and type II fibers.

On the other hand, some subjects had a rather low number of type I fibers. The reason for the high number of type I fibers in the 9 subjects could be a transition of fibers from type II to type I. This finding also has been noted recently in anterior tibial muscle by Edström et al [8]. The negative correlation found in the present study between the relative occurrence of type I fibers and muscle strength indicates that subjects with a low muscle strength

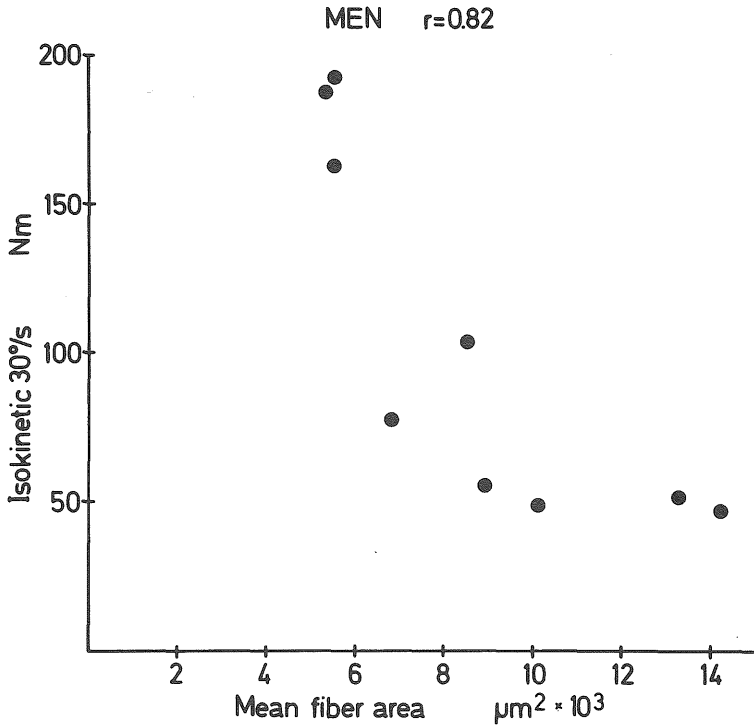


Fig. 5. Relationship between isokinetic knee extension strength, measured as peak torque at an angular velocity of 30°/s, and the mean fiber area in male post-polio subjects.

TABLE 1. Histopathologic Findings (n = 19)

	No. of Subjects
Fiber atrophy (> 10 fibers)	
type I	1
type II	4
Small angular fibers	3
Small round fibers	18
Large grouping (> 16 fibers)	
type I	12
type II	12
Internal nuclei (> 3%)	10
Splitting	8
Fibrosis	2

in the vastus lateralis must use as much of their muscle mass as possible to perform daily activities and, thus, activities that normally recruit the type I fibers. The type I fibers were also large in most of the subjects with many type I fibers. However, in some subjects, more normal and even low values of fiber size were noted. In some subjects, this could be explained by a relatively large occurrence of atrophic fibers, which reduced the average fiber size. The negative correlation between muscle strength and mean fiber area seen in the male subjects could be explained by the excessive use of the remaining muscle fibers, leading to hypertrophy; however, this was not seen in the female subjects. Such a difference could have several explanations, such as differences in physical activity and hormonal differences.

In the present study, several muscle fascicles could not be examined; therefore, the histopathologic findings should be taken with some reservation. The histopathologic findings were dominated by the occurrence of large groupings seen for both type I and type II fibers. This indicates not only a previous denervation/reinnervation process, but also a possible transition from type II fibers in subjects with a large proportion of type I fibers. Further studies of the motor unit distribution and its innervation are in progress using a single fiber electromyographic technique. Splitting and internal nuclei were seen, but not as a very dominant finding and usually only in relatively few of the muscle fibers in the specimens.

Despite the high occurrence of type I fiber, the activity of the oxidative enzyme citrate synthase was low or very low in most subjects, which is in accordance with the low physical activity of the subjects. Whether the enzymatic activity can be increased by physical training remains to be studied. Obviously, the glycolytic enzymatic activities (TPDH, LDH) were not affected similarly in most subjects.

SUMMARY

The main histopathologic finding is large grouping of type I and type II fibers. Subjects with low muscle strength had a large number of type I fibers. Large fibers were found especially in men with low muscle strength. The oxidative enzymatic activity was reduced.

The findings suggest a compensatory process, with an increased number of type I fibers in subjects, a large reduction in muscle strength, and also an increase in the fiber size. There is a sex difference in the fiber hypertrophy.

ACKNOWLEDGMENT

Thanks are due to Ms. Marita Hedberg, Gull-Britt Henning, and Elvy Lénberg for skillful technical assistance.

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DISCUSSION

DR. BRADLEY: Can you compare your data with Marinos Dalakas' data with regard to large grouped atrophy, and whether in fact you were looking at any patients who had progressive muscle weakness in the muscle in which you were studying?

DR. GRIMBY: We found grouped atrophy defined as more than 10 atrophic fibers of the same type grouped together in 4 of these 19 subjects. About one-fourth of our subjects did not report any increasing symptoms. Three-fourths have reported it over the last years, and we could not find a significant difference between these 2 groups in any of our measurements. One reason might be that the group of subjects who did not report any symptoms was small: only 5 of the 19 subjects.

DR. BROSTOFF: You showed an inverse correlation between strength and mean fiber area. Does that suggest that hypertrophy results from a loss of fibers and purely reflects a smaller number of muscle fibers?

DR. GRIMBY: The hypothesis from the findings would be that these subjects with the lowest muscle strength have a reduced number of motor units and also muscle fibers. With a relative overload of these remaining motor units, the muscle fiber hypertrophy seems to be able to cope with the needs of daily life.

Strengthening Exercise Program in Post-Polio Subjects*

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INTRODUCTION

In Sweden, most polio survivors now have a post-polio history exceeding 25 years. According to recent epidemiologic studies [1–4], many post-polio subjects suffer from a variety of late sequelae presumably caused by their post-polio condition. Most of these studies indicate that muscle changes are the common denominator of the problems appearing some 30 years after the onset of polio [5]. Several hypotheses have been offered to explain the nature and background of the muscle changes [6]. There is a shortage of knowledge concerning the structure of post-polio muscles and the adaptability of these muscles to activity.

Studies of possible programs to prevent muscle overload are of paramount importance for health maintenance in polio survivors. Quoting Richard L. Bruno, . . . “the recurring questions concerning the effect of exercise on unaccustomed fatigue and impaired muscle functioning, whether it is deleterious, therapeutic, or both, have not been answered empirically” [7]. The present study is a first attempt to study the possibility of increasing muscle strength by a well-controlled, high-intensity, strengthening training program, and to seek objective measurements to demonstrate positive and negative effects in a group of post-polio subjects.

STUDY POPULATION

Twelve subjects were chosen from a Gothenburg study of 41 polio survivors [8]. These survivors were quite similar to polio patients investigated

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in earlier surveys [1, 3] regarding the periods of improvement, best function, and deterioration. The subjects in the training study were 5 men, 43 to 61 years of age, and 7 women, 41 to 63 years of age. The study was performed 24 to 61 years after onset of their polio. They had markedly weakened knee extension, but could perform a full knee extension against gravity. They were walkers, even if some of the subjects also used wheelchairs. Nine of the 12 subjects described a post-polio syndrome-like reduction in physical function occurring 2 to 15 years before the study.

METHODS

General Assessment

The 12 polio subjects had undergone a clinical examination and assessment of ADL functional capacity and social performance (to be published separately). Manual muscle tests (MRC- 0–5 scale) of all affected muscles were done. All subjects had knee extension grade 3+ and above.

Muscle Strength

Muscle strength for knee extension and knee flexion was measured before and after training using a modified Cybex II muscle dynamometer with a specially designed computer program, including compensation for the torque due to the weight of the lower leg and lever arm of the dynamometer [9]. Isometric muscle strength was measured in knee extension at 30° and 60° knee angle, isokinetic strength during knee extension, and knee flexion with angular speeds of 30°, 60°, 180°, and 300°/s. Peak torque values are reported.

Muscle Biopsy

Muscle biopsies were taken before and immediately after the training program from the vastus lateralis muscle of the trained leg. A standard conchotome (alligator forceps) was used for collecting the muscle samples, which were taken from as near the same part of the muscle as possible on both occasions. The procedure was performed under local anesthesia. The muscle specimens were divided into 2 parts: one part was frozen immediately in liquid nitrogen to be used for analyses of enzymatic activities; the other part of the sample was trimmed, mounted, and frozen in cold isopentane to be used for histochemical analyses. Both parts were stored at –80°C until analyzed. The myofibrillar ATPase method was used for muscle fiber classification, with subclassification of type II fibers into type IIA and type IIB. The fiber area was measured and NADH activity, stained, transverse sections were photographed using an optical illumination device. Histopathologic evaluation was made using hematoxylin-eosin and modified Gomori-trichrome staining. For

further methodologic details, see the preceding paper on the same group of subjects [8].

For biochemical assays, the enzyme activity was determined by means of fluorometric techniques using a Farrand ratio-fluorometer-2 (Farrand Optical Co, NY). The reactions catalyzed by the enzymes under investigation were coupled to NAD-NADH-linked reactions and determined according to the principles given by Lowry and Passoneau [10]. Triose-phosphate-dehydrogenase (TPDH), lactic dehydrogenase (LDH), myokinase (MK), and citrate synthase (CS) were analyzed. The assays were performed at $+37^{\circ}\text{C}$. The protein content was determined in order to express the activities per gram protein.

Muscle Training

Before each training session, a standardized warm-up program was used with 5 minutes on a bicycle ergometer at a load of 30W. The training program was performed on the Cybex II isokinetic dynamometer with 12 sets of 8 isokinetic contractions each at $180^{\circ}/\text{s}$ angular speed interposed with 12 sets of isolated 4 sec isometric contractions, as shown in Table 1. The time for isokinetic work added up to 16 seconds/group of sets = $16 \text{ sec} \times 3 = 48 \text{ sec}$, which corresponds to a total time for isometric work of 48 sec. Thus, time consumption for contractions during each session was 96 seconds. All 12 subjects performed the training program in 6 weeks with 3 sessions per week.

TABLE 1. Training Program

First group of sets:
1. isokinetic: 8 contractions at $180^{\circ}/\text{s}$ angular speed resting 10 sec
1. isometric: 1 contr at 60° knee angle during 4 sec resting 10 sec
2. isokinetic: 8 contr at $180^{\circ}/\text{s}$ angular speed resting 10 sec
2. isometric: 1 contr at 30° knee angle during 4 sec resting 10 sec
3. isokinetic: 8 contr at $180^{\circ}/\text{s}$ angular speed resting 10 sec
3. isometric: 1 contr at 60° knee angle during 4 sec resting 10 sec
4. isokinetic: 8 contr at $180^{\circ}/\text{s}$ angular speed resting 10 sec
4. isometric: 1 contr at 30° knee angle during 4 sec
5 min interval
First group of sets repeated
5 min interval
First group of sets repeated

An interview concerning symptoms at exercise, general well-being, and strength was made after the training period, and 5 to 12 months later.

Statistics

For statistical calculations, nonparametric methods (Wilcoxon's signed rank test and Spearman's rank correlation tests) were used.

RESULTS

There was a significant ($P < 0.01$) increase (average 29%) in isometric knee extension muscle strength measured at 60° knee angle and in isokinetic knee extension strength (average 24%), measured as peak torques at angular velocities of 30° to 300°/s (Fig. 1). The peak torque values did not decrease significantly 5 to 12 months after training in the various measurements. Measurements of isometric and isokinetic strength for knee flexion—not trained—did not show any significant differences before and after the training period.

As seen in Table 2, 10 of the 12 subjects reported a feeling of increased strength in the trained leg after the training period, and in half of these 10 subjects, this feeling was limited to the trained leg. Seven of the subjects reported a feeling of strength in the trained leg even 5 to 12 months after the training period ended, whereas 3 subjects reported maintaining strength for 1 to 3 months post-training. It is noteworthy that all subjects performed all training sessions within a planned period of 6 weeks without discomfort that could limit training ability.

There was no significant evidence of a change in fiber composition or fiber areas with training. However, due to the sample heterogeneity of the morphology, and the use of only one biopsy at each sampling time, detection of structural differences could not be expected. After training, there was no indication of a higher occurrence of histopathologic findings in the biopsies. The enzymatic activity of CS showed a significant increase ($P < 0.05$) with training, as seen in Figure 2. No significant changes were found in the other muscle enzymes studied.

DISCUSSION

The present study evaluated the possibility of achieving training effects by a high intensity strength training program in muscles affected by poliomyelitis decades earlier. Most of the subjects had experienced reduced function, not specific to any particular muscles, during the years before the present study. It is noteworthy that in this group of polio subjects with rather marked muscular weakness, the present strength training program could be completed

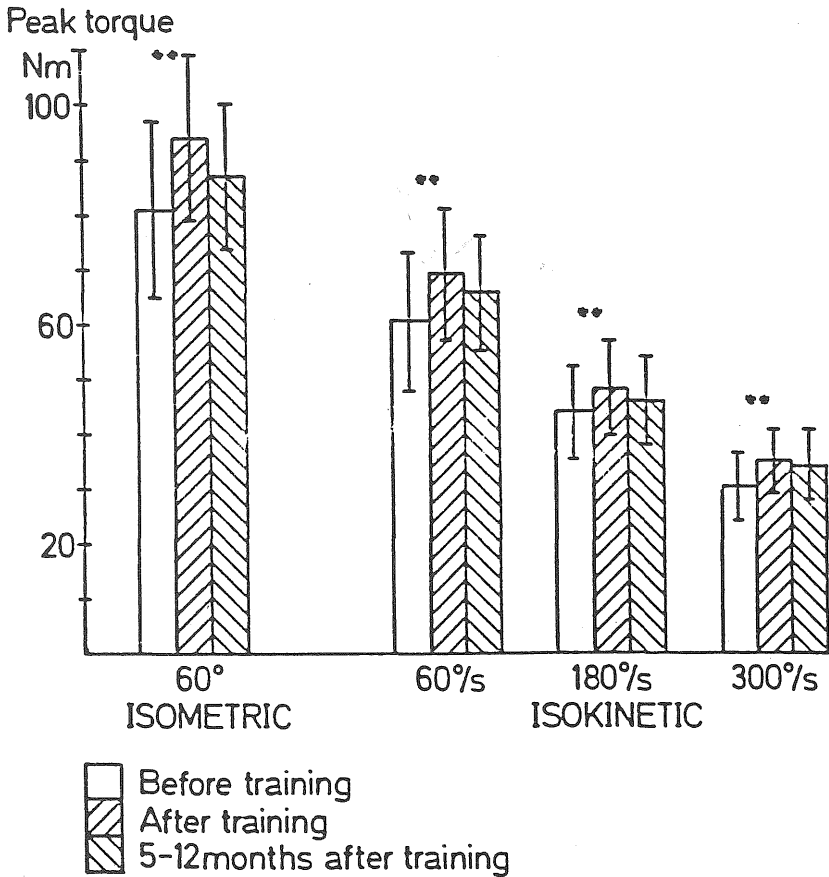


Fig. 1. Maximal torque during isometric knee extension with a knee angle of 60° and peak torques during isokinetic knee extension with angular velocities of 60°/s, 180°/s and 300°/s in 12 post-polio subjects before, immediately after, and 5 to 12 months after a 6-week period of strengthening exercise of the quadriceps muscle.

TABLE 2. Interview 5-12 Months after Training (n = 12)

	Yes	No
Increased feeling of well-being during training	9	3
Increased feeling of well-being after the training period	8	4
Feeling of increased strength in the trained leg immediately after the training period	10	2
General feeling of increased strength after the training period	5	7

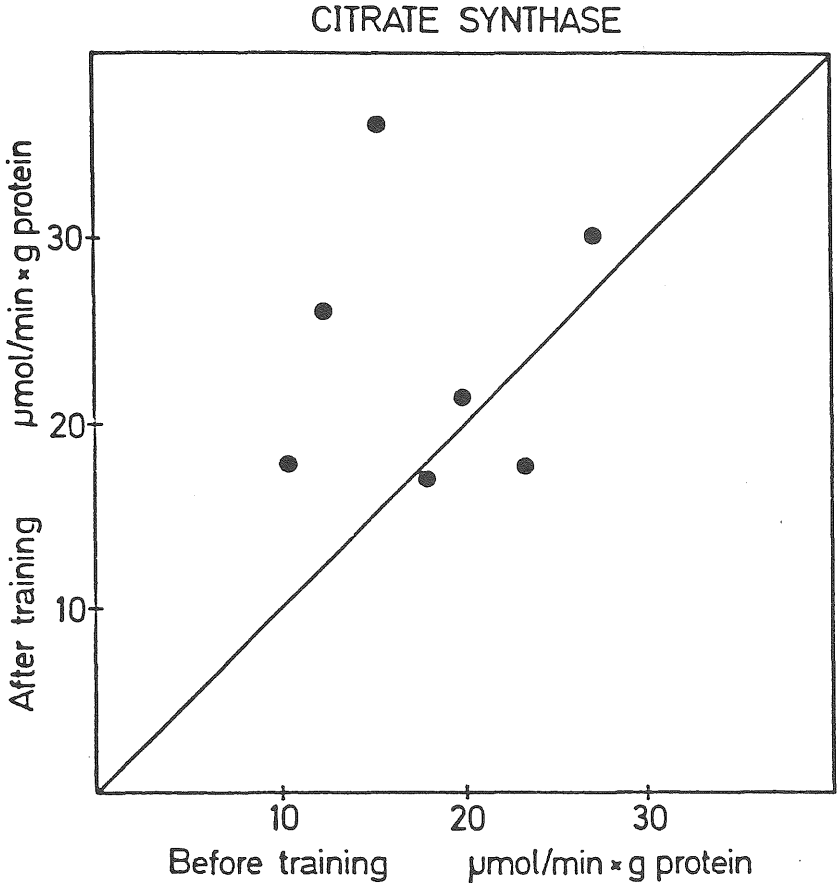


Fig. 2. Changes in enzymatic activity of the oxidative enzyme citrate synthase (CS) after 6 weeks of strengthening exercise of the quadriceps muscle in 7 post-polio subjects.

without any discomfort or evidence of negative effects. Their pretraining strength values on the average were rather low and less than half of expected values [8]. When both legs of the subjects were affected, the weakest quadriceps muscle was trained, provided it could perform a resisted full knee extension.

No control group was studied, but the lack of change in muscle strength in the untrained knee flexors over the same period of time indicates true training-induced changes. It is not possible to evaluate whether the training effects are specific for the type of muscle contraction used in training because the same type of contraction also was used for testing. In this model, we chose to study the quadriceps muscle because a standardized training program for

knee extension could be performed and biopsies could be taken from the vastus lateralis muscle where reference values are available. An increased muscle strength would also be of practical value for performing various daily activities requiring knee extensor strength.

Since previous studies of strength training in post-polio subjects have had a different design [11, 12], no detailed comparison can be made. The general conclusion from these studies and the present study is that there are subjects with rather marked muscle weakness after polio who can improve their strength, evaluated objectively as well as subjectively, from a period of muscle training. The long-term effect is naturally unknown, but evidently, the increased strength can be maintained at least for a period after the end of the program. A possible explanation is that ordinary daily activities, such as rising from a chair, climbing stairs, and walking, now can be performed more easily, and therefore, the quadriceps muscles were being used more than before the training started.

The increase in oxidative enzymatic activity can be explained on the basis of the increased metabolic activity during and between the contractions. Those contractions were of long enough duration to result in an adaptation with increased oxidative capacity in the muscle. A similar finding after training was noted by Grimby et al [13] using a series of short maximal contractions and short resting periods between each contraction. The pretraining value of CS was low or very low in most subjects [8], and the increase in the CS activity indicates increased muscular endurance. Such a training effect has important implications for the functional capacity in daily activities and therefore should be studied further using special endurance training programs of different muscle groups in functional activities.

The present study was supplemented with recordings (together with Erik Stålberg) of single-fiber EMG and macro EMG to record motor unit size and distribution and to detect possible evidence of instability in the motor unit, which could have an impact on the training procedure. These results will be published separately.

ACKNOWLEDGMENTS

Thanks are due to Ms. Marita Hedberg, Ms. Gull-Britt Henning and Ms. Elvi Lénberg for skillful technical assistance.

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DISCUSSION

DR. FELDMAN: Was there any period of training at all during the 12 months after your initial training period before your reevaluation?

DR. EINARSSON: No organized training program was prescribed. Most of the patients told me that they were more active than before and one could maybe conclude that the activities of daily living that they were able to do to a greater extent than before would be their training.

DR. GRIMBY: These are the same subjects I have shown in my slides. So, quite a majority of the subjects in the training study already have large fiber areas, meaning they have actually trained before the training program started.

DR. FUGL-MEYER: I have 3 reasonably short questions for you. First of all, on the training, did you set some actual goal for each training period? Did the subjects increase in their peak torque, and could the increased strength simply be learning?

DR. EINARSSON: The answer to the first and second questions is no. Dr. Grimby will answer the third question later. The main thing is that they maintained at least half of their increased strength from the training.

DR. WIECHERS: How can you be sure that with the type of exercise program

you are prescribing that you are not strengthening the other quadriceps muscles, the rectus femoris or the vastus medialis?

DR. GRIMBY: The strengthening/training program was for knee extension. All muscles involved in the extension are activated and trained. Vastus lateralis was of interest only for the biopsy studies with respect to the effect of training. It demonstrates that there might be or there could be metabolic adaptation with this type of training program with the repeated sets of contractions. All the other data, namely the strength measurements, are for the whole knee extension. Concerning learning, we don't know what role it plays because that was difficult to evaluate by muscle biopsies or by any other type of measurement.

DR. WIECHERS: It looks like we can improve the strength of our patients with these exercise techniques. I am concerned that we may have just cost these persons 2 additional years of ambulation by hyper-functioning their residual motor neurons to gain this strength. In other words, will exercise have a negative effect in 5 years?

DR. GRIMBY: Yes, that was part of my concern too. This study demonstrates adaptability for a certain group of polio patients to increase strength and probably also some metabolic factors in the muscle. These patients are already training their muscles to quite a large extent, and then they train and continue to use their muscles and hopefully maintain what they achieve. I think, before putting this into a clinical situation, there should be a much broader training program involving both strength and endurance training to demonstrate the short-term and long-term effect. It could take years to know who should train and who should not train.

DR. MUNSAT: Do you believe that it is possible that part of the neuromuscular post-polio syndrome actually resides in the muscle fiber, and that in some way, we could alter the rate of deterioration by an exercise program?

DR. EINARSSON: The only thought I have had is that you might use the capacity still in the muscle more effectively.

Excessive Use of Remaining Anterior Tibial Motor Units During Locomotion and Absence of Type II Muscle Fibers in Antecedent Polio*

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It has been shown in animal experiments that long-term electrical tetanization causes a transition of type II to type I fibers and that muscle fibers as phenotypes are reflections of their long-term use [1].

Since leg muscles are used predominantly for locomotion, walking at free speed should reflect the long-term use of a motor unit in a leg muscle. When a normal human subject walked at ordinary speeds, the motor units in musculus tibialis anterior (TA) with the lowest threshold fired 5 to 10 times in each step cycle at intervals corresponding to rates between 10 Hz and 25 Hz. Units with moderately high thresholds fired only once or a few times at 20 Hz to 25 Hz in each cycle. The units with the highest thresholds did not participate in each step cycle, but fired in short, high frequency bursts in diverging strides and during corrective movements [2, 3]. In the normal TA muscle, 60% to 80% of the fibers were type I and 20% to 40% type II [4].

In neuromuscular disorders, remaining motor units were overused to compensate for the loss of muscle tissue. In half of the patients with foot drop because of acute unilateral peroneal palsy, all remaining TA units fired for several hundred milliseconds at rates that should be sufficient for full fused power in each step cycle [3]. The aim of the present study is to elucidate the overuse of remaining low and high threshold TA motor units during walking in subjects with a history of polio, and the consequences of long-term overuse for the TA muscle fiber differentiation.

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MATERIALS AND METHODS

The use of the TA muscle was studied during walking at free speed with electromyographic (EMG) techniques in 18 patients with paralysis of the foot dorsiflexors 25 to 53 years after polio (median 40). The patients were 5 to 37 years of age (median 19) at the acute stage of the disease and 37 to 71 years (median 58) at the examination. None of the subjects had any marked progression of muscle atrophy.

Recordings of just one TA motor unit during locomotion were obtained by special wire electrodes equipped with a hook for fixation in the muscle [2], or by superficially located thin needle electrodes, or surface electrodes. In antecedent polio, there were no major technical difficulties since the number of motor units was decreased and the muscle fiber density within the remaining units increased. That only one motor unit had been recorded could be verified by observing that the shape of the potential evoked by supramaximal electrical stimulation of the peroneal nerve was identical to the voluntary one. Confusion of potentials originating from different units could also be excluded since they had characteristic shapes because of reinnervation.

Recordings of the global TA were obtained by Medelec or Beckman surface electrodes, and the rectified signals were integrated in a linear way. The recording electrodes were connected to a small pre-amplifier strapped to the leg and connected to the main amplifier by a cable permitting 40 meters of indoor locomotion and wireless walking outdoors. The EMG activities were related to the signals from 2 tape switches, one strapped to the heel and the other to the anterior part of the shoe. The 2 switches operated at different voltages so that the signals could be distinguished when recorded simultaneously. The subjects used their ordinary light weight summer shoes with low heels.

Biopsy of the TA muscle by a percutaneous conchotome method was performed in the 18 walking polio subjects and also in 3 wheelchair-bound polio subjects. The biopsy material was quickly frozen in Freon cooled by liquid nitrogen (-190°C). Cryostat sections were treated by a battery of stainings and the fiber type classifications were based on myosin ATPase characteristics according to Brooke and Kaiser [5]. Most biopsies contained 400 to 500 fibers.

RESULTS

Identification of Motor Unit Type

In the normal TA, *low threshold units* responded tonically to weak voluntary drive at rates lower than 10 Hz, while *high threshold units* responded tonically only when the drive was close to maximal and then only at

rates higher than 20 Hz. There was a continuum between the 2 extreme types, and the term *intermediate* will be used for units with a minimal rate of about 15 Hz [6].

In previous studies we have shown that the voluntary minimal rate of a motor unit was closely correlated to its axonal conduction velocity [7], its contraction time [8], and its fatigability [9, 10]. The correlation between minimal rate and axonal conduction velocity was also observed in spinal muscle atrophies [11].

Also in antecedent polio, there was a differentiation of motor units into low threshold units capable of firing at rates below 10 Hz, high threshold units only firing at rates above 20 Hz, and intermediate threshold units, as well as a close correlation between minimal rate and axonal conduction velocity. The maximal axonal conduction velocities were as high as in normal subjects [12].

To get an index of the proportion of low and high threshold TA units, the firing rate of a low threshold test unit was compared to the integrated surface electromyogram (EMG) while voluntary tension was increased slowly to maximum. When a test unit in a normal subject fired at 10 Hz, the global EMG was less than 10% of that recorded during maximal tension. At 15 Hz, the global EMG was about 20% of maximum and at 20 Hz, about 50%. The findings indicate a recruitment of new units throughout the frequency range of the low threshold unit, with a peak between 15 Hz and 20 Hz. In each of the polio subjects in whom the TA muscle fiber differentiation was lost (cf below), the relation between the firing rate of low threshold unit and the global EMG was studied. The findings indicated a recruitment peak between 15 Hz and 25 Hz.

The Use of Low and High Threshold TA Units During Walking

When a normal subject walked at ordinary speed, only low threshold units fired during most of the swing phase and then at rates between 15 Hz and 25 Hz. Intermediates fired once or a few times per stride at the heel strike. High threshold units did not participate in the stride [3].

Paralyzed subjects compensated during walking for the loss of TA tissue by increased recruitment, firing rates, and firing duration of remaining TA units and/or by changed pattern and speed of gait. The overuse of remaining TA units in the step cycle was most marked in subjects with a moderate TA paralysis (Kendal 3–4) and only slight weakness of other leg muscles. Since most of these subjects are as physically active as many normal subjects, the number of steps per day should not be markedly decreased. Subjects with minor TA weakness (Kendal > 4) could walk in a normal way without significant overuse. Subjects with so severe TA paralysis (Kendal < 3) that they could not achieve a heel strike tended to change from a plantigrade to a

digitigrade gait pattern so that the TA muscle was partially protected from abnormal strain. Subjects with severe paralysis of several leg muscles usually walked so slowly that the strain on the TA muscle was low.

When polio subjects with a critical degree of TA weakness walked at free speed, both high and low threshold TA units fired at 20 Hz to 30 Hz for most of the swing phase and attained 40 Hz to 50 Hz at the heel strike in each stride, ie, at rates close to those during maximal voluntary tension [3]. Figure 1 illustrates the firing common to all remaining motor units during ordinary walking in such a polio subject. The unit in the figure fired at about 25 Hz during the swing phase and 50 Hz during the heel strike. Differences in firing between the motor unit types became apparent only when the drive was not sufficient for the minimal rate of high threshold units, eg, during reduced speed of walking.

Biopsy Findings

In 20 middle-aged control subjects (median age 59) the percentage of type I fibers was 57 to 90 (mean 73) [14]; ie, middle-aged subjects did not differ markedly from younger subjects dominating the most normal materials.

In 9 polio subjects, there was no marked overuse during walking (the quotient between the global TA EMG recorded during walking and that

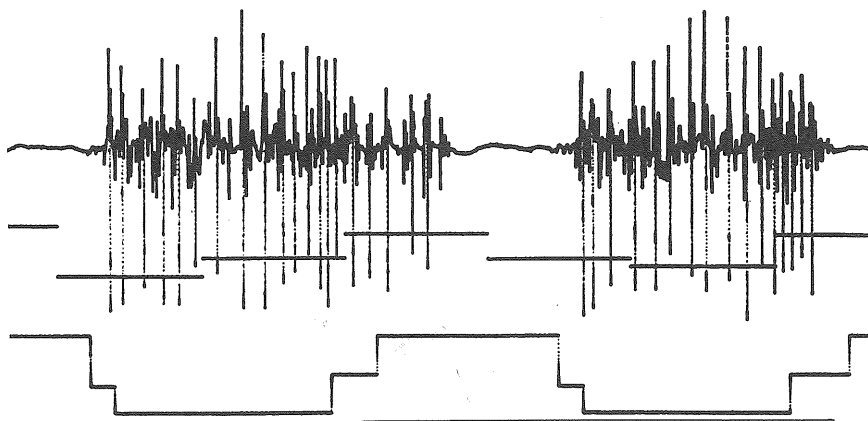


Fig. 1. Upper trace shows the firing pattern common to all remaining single TA units during walking at free speed in a polio subject. Middle trace shows the global TA EMG integrated over periods of 300 milliseconds and displayed during the following period. Lower trace shows signals from foot switches. High amplitude upward deflexion denotes pressure on the whole sole of the foot, intermediate amplitude pressure only on the heel, and low amplitude pressure only on the toes. Time bar 1 second.

recorded during maximal voluntary tension was less than twice the normal one). In the biopsies from these subjects 53% to 100% (median 82%) of the TA muscle fibers were type I. Most fibers were of normal size and shape (Fig. 2a).

In 8 moderately paralyzed, middle-aged polio subjects (median age 58), there was a marked overuse of remaining TA units during walking (the EMG quotient was 3 to 4 times normal). In the biopsies from these subjects, almost all TA fibers were type I (83% to 100%, median 100%) [15]. Most fibers were of normal size and shape, and only one biopsy specimen exhibited pronounced fiber splitting (Fig. 2b).

Four polio subjects had such severe paralysis that remaining muscle tissue was useless. Three subjects were wheelchair-bound and one "walked" with braces without using residual TA motor units. In their biopsies, there was no type I fiber predominance (type I 10% to 60%, median 29%). Fibrosis and muscle fiber atrophy were marked. Many muscle fibers exhibited splitting, central nuclei, myofibrillar disorganization, and other structural changes.

COMMENTS

Polio subjects who walked in a fairly normal way by using all remaining TA units tonically in each stride had almost only type I TA muscle fibers. On the other hand, subjects who were so severely paralyzed that remaining TA units were useless had a differentiation into type I and II fibers.

The loss of muscle fiber differentiation cannot be due to the disease per se since the most affected muscles were differentiated. The distribution of the muscle fiber types is nonuniform in chronic neuromuscular disorders because of collateral sprouting. However, the absence of type II fibers cannot be due to a sampling error since the biopsy material was ample and the finding reproduced in all 9 subjects overusing remaining muscle fibers. Motoneurons with high threshold and high axonal conduction velocity normally innervate type II muscle fibers. There were no signs of a selective loss of such motoneurons in antecedent polio [12].

We suggest that the excessive use during locomotion causes a transition of the muscle fibers innervated by such motoneurons from type II to type I. This hypothesis is supported by the finding that type II TA fibers are also absent in other neuromuscular disorders characterized by foot extensor weakness, ie, Welander disease [16, 17], and myotonic dystrophy [18].

To elucidate whether long-term excessive use might be harmful for remaining motor units, we are planning a follow-up of polio patients who use their units to such an extent that type II fibers are transformed, and another less mobile group with differentiated muscle fibers.

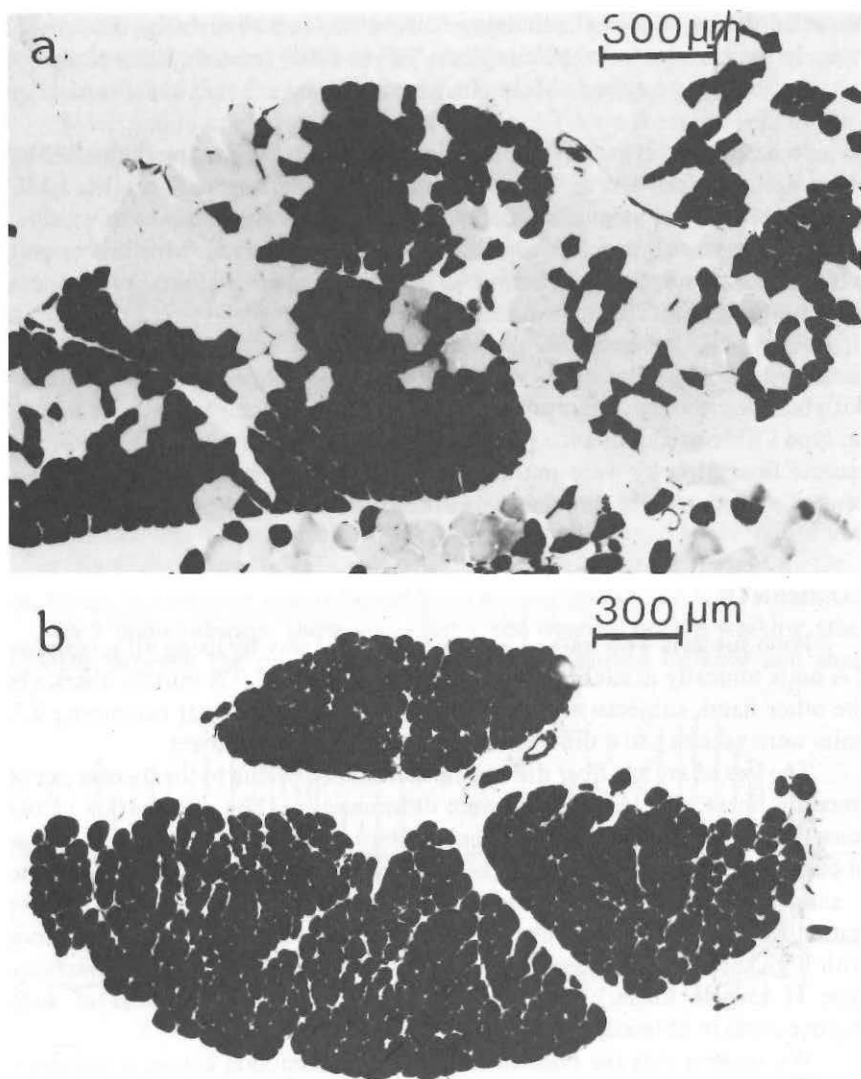


Fig. 2. Cryostat sections from anterior tibial muscle biopsies obtained from one polio subject with ordinary use of the muscle (a) and one subject with overuse of the muscle (b) during locomotion. The sections are stained for myosin ATPase after acid preincubation (pH 4.3). In (a), there is a differentiation between type I fibers (darkly stained) and type II (unstained). Both types of fibers are found in abundance and some slight type grouping is seen. In (b), only type I fibers are observed.

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DISCUSSION

DR. DALAKAS: Initially on some biopsies there was significant grouping of Type I fibers and when you rebiopsied you found only Type I. Since we know that needle biopsy is notoriously unreliable to detect grouping as it is a small specimen, if you had done an open biopsy or had gotten a bigger piece, could you have possibly seen that this may not have been the case?

DR. BORG: Well, I can give you an answer to this question. In the material of 21 conchotome biopsies (there were no needle biopsies), we had 9 with 100% type I fibers, and the number of fibers were sufficient enough to judge that the type I fiber dominance was not due to type grouping.

DR. WIECHERS: I would like to ask a question about your placement of the wire electrodes for identifying the motor units. Was this a random placement or did you manipulate it to get near one or the other unit, and did you record from more than one site in the muscle? Which unit you are looking at may be fairly critical.

DR. GRIMBY: The wire electrode is inserted into a large cluster of muscle fibers innervated by one motor neuron. When we have a sufficiently large cluster to record just one motor unit during maximal contraction or supermaximal electrical stimulation, we leave the electrodes there and if we are lucky, the recording remains during walking for considerable periods of time. We can define different types of clusters—clusters belonging to low-threshold motor neurons and clusters belonging to high-threshold motor neurons—and we can determine velocities of their motor axons and thus identify the type of motor neuron.

Investigations of Neuromuscular Performance in Post-Polio Patients: A Practical Approach

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Fatigue can present as a late effect of poliomyelitis, but its causes and mechanisms are not understood. Loss or atrophy of motor units causes post-polio weakness and fatigue, which are often of late onset.

Physiologic measurements are necessary for identifying the factors contributing to fatigue, as manual clinical tests are imprecise. This review describes techniques for assessing motor performance, which may be affected at any point in the chain of command for voluntary muscle contraction (Fig. 1).

CLINICAL INVESTIGATIONS

A detailed clinical history is necessary to establish the patient's physical status before contracting poliomyelitis, and also to determine the extent of residual weakness when the acute infection subsided. Clinical examination is aimed at determining whether present symptoms might be related to a pathology other than previous poliomyelitis. The extent of the previous disease can be estimated by routine electromyography (EMG) and needle muscle biopsy [1]. Functional limitations related to the disability mean that greater effort or energy expenditure may be required for activities of daily living (ADL). For example, abnormalities of walking can be examined by formal gait analysis [2], and then used to assess the suitability and effect of orthoses to improve the metabolic cost of walking. Facilities for gait analysis are not widely available, but walking aids such as a stick or knee brace [3] should be considered for patients with abnormal gait on clinical examination.

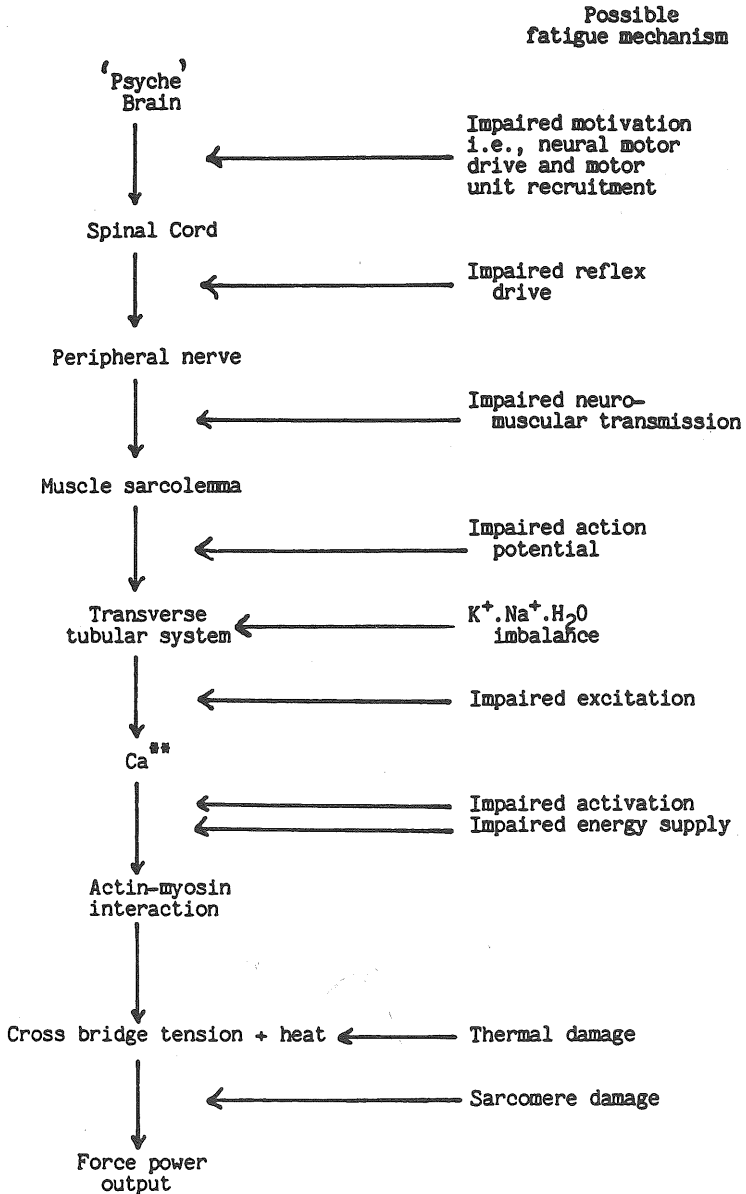


Fig. 1. Chain of command for muscular contraction and the possible mechanisms underlying fatigue. (Adapted from Edwards [21].)

PHYSIOLOGIC MEASUREMENTS

Muscle Weakness

Weakness is defined as failure to generate force or power output. Possible causes include loss and/or atrophy of motor units, failure of motor unit recruitment, or abnormalities in units recruited. Force generated during isometric maximal voluntary contractions (MVC) can be measured accurately by strain gauge dynamometry. Quadriceps MVCs correlate well with body weight [4] and even more closely with quadriceps cross-sectional area (measured by ultrasound scanning) [5].

Isokinetic force can be measured using more sophisticated devices such as the Cybex, which also has an isometric mode. Since many post-polio patients complain of pain as well as fatigue, isometric testing is more appropriate as efforts are less likely to be restricted by pain. The Cybex system has proved valuable in investigating force:velocity relations of muscle and in certain forms of rehabilitation exercise. It offers no advantages for the present studies, however, which include electrical stimulation.

Joint damage associated with muscle weakness and joint instability may cause reflex inhibition of muscle contractions [6]. The contribution of inhibition to weakness can be assessed by measuring muscle size and strength [7], and voluntary and reflex activation by surface EMG and H-reflex testing [6, 8].

Cycle ergometry is a useful means of assessing cardiorespiratory fitness provided there is no serious asymmetry of muscle strength in the lower limbs or local joint deformity that would interfere with cycling action.

Muscle Fatigue

Fatigue is the failure to maintain a given force or power output during sustained or repeated contractions. This is to be distinguished from a feeling of "fatigue" in the absence of any muscular activity.

Central fatigue. This is due to a failure of neural drive and may be due to lack of motivation or an impairment proximal to or involving recruitment of the motoneuron. Central fatigue can be demonstrated using the interpolation of twitches [9, 10] or tetany at different frequencies [11] in the course of a voluntary contraction. The twitch interpolation technique involves superimposing electrical stimuli at 1 Hz during voluntary contractions of different strengths. Force is only increased by the twitches when voluntary contractions are submaximal (Fig. 2).

Another aspect of central fatigue is perception of effort of voluntary contractions (normal responses were studied in normal subjects by Borg [12] and Cooper et al [13]). An increased effort associated with performing simple, familiar motor tasks is a striking complaint in patients with hemiplegia [14].

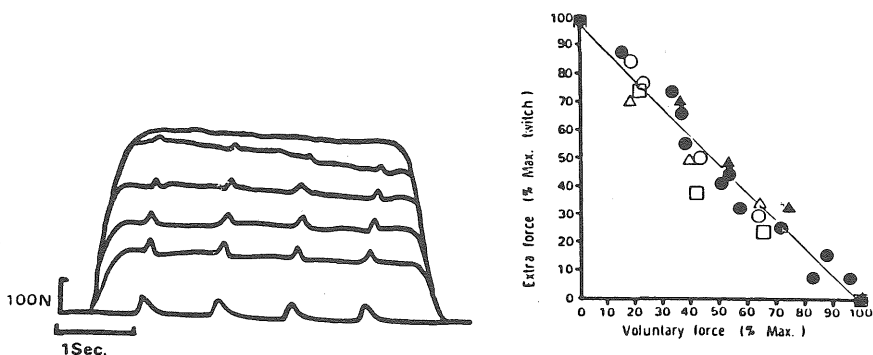


Fig. 2. Extra force generated by interpolated twitches during voluntary contractions at various forces in the quadriceps muscle in a normal subject.

Peripheral fatigue is due to failure within the periphery of the motor unit (Fig. 1) and is demonstrated by testing the contractile properties of the muscle during stimulated contractions [4]. The frequency:force relationship and relaxation characteristics are examined by percutaneous supramaximal stimulation of motor nerves delivered in a set pattern of frequencies. The force and EMG records produced are termed the “programmed stimulation myogram” (Fig. 3). The quadriceps muscle is stimulated via the motor end nerves and the adductor pollicis is stimulated via the ulnar nerve at the wrist. Fatigue can occur at high or low frequencies depending on the causal mechanism and site of impairment (Table 1).

Pain

There is a need to distinguish between fatigue and pain in muscle, whether originating from muscle or referred from bony structures, as might result from prolonged or unphysiologic postures caused by muscle weakness.

DISCUSSION

Investigations

The physiologic and clinical tests described can be used to form a comprehensive assessment of motor performance in post-polio patients. Measurement of perception of effort and heart rate during cycle ergometry examines the appropriateness of physiologic and psychologic responses to graded exercise under controlled conditions. This also has the advantage of showing the patient that it is safe to exercise, thereby building his/her confidence and serving as a “therapeutic” exercise test. Measurements of muscle fiber size and whole muscle cross-sectional area (CSA) indicate whether weakness is due to loss or atrophy of fibers. Relating body weight to

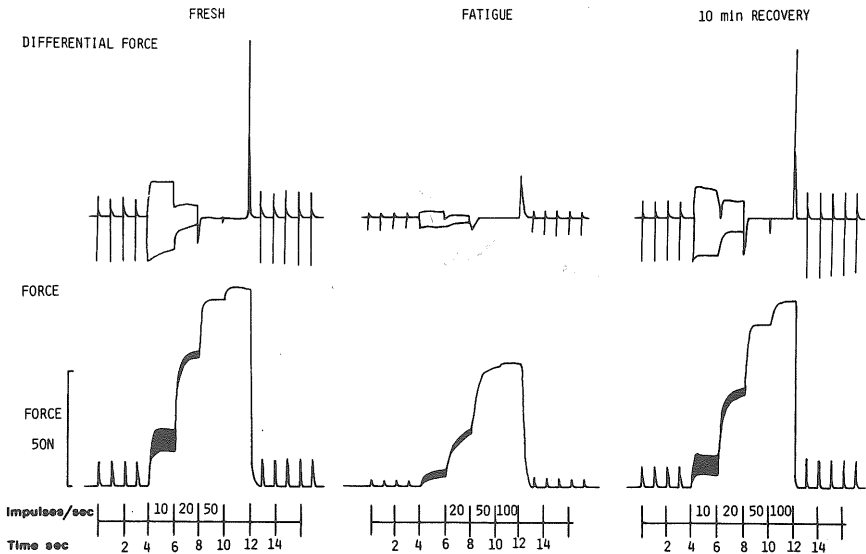


Fig. 3. This demonstrates programmed stimulation myogram (PSM) of adductor pollicis. The lower trace is the force record of contractions during stimulation at different frequencies: 1, 10, 20, 50 and 100 Hz. The upper trace is the differential force signal (indicating rate of change of force) that is used to calculate maximal relaxation rate. Immediately after fatigue, force is reduced at all frequencies but with recovery, returns to normal. However, the force at low frequency, 10 and 20 Hz, takes longer to return to normal and thus the 10:50 or 20:50 Hz ratios may be used to assess fatigue.

TABLE 1. Physiologic Assessment of the Symptom of Fatigue: Fatigue or Weakness?

Central fatigue?	Use of electrical stimulation eg, twitch interpolation technique to determine whether contraction is maximal. If not, "central" fatigue is suggested.
Peripheral fatigue?	Classified according to whether elicited with high or low frequency stimulation indicating impaired neuromuscular transmission/sarcolemmal excitation or excitation-contraction coupling, respectively.
Metabolic accompaniments of fatigue	Measurements of plasma lactate during or after muscular activity. Interpretation depends on comparisons made at same absolute and relative forces or power outputs.
Therapeutic trial	"Prescription" of a pedometer and keeping of a diary of physical activities with pedometer readings.

force per unit fiber area allows estimation of expected forces generated and the possibility of fatigue or damage occurring due to excessive forces. Weakness in the absence of pain that is inappropriately low for the size of the muscle may indicate reflex inhibition [7] or may be due to lack of motivation. These two possibilities can be distinguished by examining the excitability of the motoneuron pool using the H-reflex [8].

Possible Mechanisms of Fatigue

It has been suggested that the effects of aging may exacerbate symptoms of weakness and fatigue in post-polio patients. Tomlinson and Irving [15] however, believe the symptoms are unlikely to be due to the loss of motor units that occurs with normal aging, but rather to the previously damaged motoneurons being more susceptible to cell death with increasing age. Because weak muscles work more closely to their maximum force/metabolic limits, they are closer to the point where fatigue occurs. This reduces the endurance capacity of the muscle to produce force, partly due to local constriction of the muscle microcirculation impeding oxygen transport. Central fatigue may be due to impairment of the ability to increase motor unit firing frequency, but clear evidence of this has yet to be demonstrated. However, a failure to sustain firing frequency has been observed during contraction in patients with partially denervated muscle [16]. This is compounded by a more extensive loss of motor units than is appreciated from clinical examination [17].

Management

Weight control is vitally important to minimize gravitational stresses on weak muscles and therefore reduce fatigue and risk of damage [18]. Cardiovascular fitness should be improved by supervised endurance training programs and monitored by exercise testing. Assessment of the psychologic profile may reveal factors that may be contributing to or perpetuating fatigue, eg, anxiety, depression, stress.

TABLE 2. Order of Symptoms Common to Patients With Post-Polio Syndrome and Effort Syndrome

Post-Polio Symptoms	Effort Syndrome Symptoms
1. Fatigue	Pain in the back and neck
2. Weakness in previously affected muscles	Muscle pains
3. Muscle pain	Fatigue
4. Joint pain	Depression
5. Weakness in previously unaffected muscles	Loss of concentration
6. Breathing difficulties	Physical weakness
7. —	Breathlessness

High levels of habitual exercise appear to protect against the development of the symptoms of post-polio syndrome in that active post-polio wheelchair athletes do not appear to complain of these symptoms [19]. A positive physiologically based management policy would appear to offer the best opportunity of dealing with the troublesome features of the post-polio syndrome. This approach is exemplified in the case of effort syndromes [20] which share several common features with post-polio syndrome (Table 2).

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DISCUSSION

DR. DALAKAS: I want to make a general comment on the needle biopsy. A needle biopsy is not the right way to do biopsy in post-polio patients. The specimen is too small to count the fiber type groups. It was pointed out yesterday that the fiber type groups in post-polio muscles are large, up to 170 muscle fibers per group. If you take a small specimen, you can really miss a lot of things. In post-polio patients, we have to do open muscle biopsies.

DR. GOW: Would you accept that repeated or multiple samples of needle muscle biopsy might be more acceptable to the patient, particularly if one wants to do sequential studies?

DR. DALAKAS: I am not sure if multiple specimens are the answer. Certainly it is easier for all of us to do needle biopsies, and this is the way to go if we want to do sequential studies, but for grouping, it is a problem.

Exercise Testing as a Useful Tool in the Physiatric Management of the Post-Polio Survivor

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INTRODUCTION

When a graded exercise test (GXT) is administered for diagnostic or clinical purposes it should show a relationship between the increasing work loads as a stimulus and the physiologic response to that stimulus.

A stress test or GXT can be performed for many reasons, including: 1) functional—to assess one's physiologic status; hence, an individual exercise program can be prescribed for members of, for example, a cardiac rehabilitation program or an adult fitness program; 2) diagnostic—to assist in one's medical diagnosis; 3) therapeutic—to develop conditioning programs for professional athletes, etc; and 4) discharge planning—to assess the cardiovascular efficiency, symptoms, and medication changes of a patient before discharge from the hospital.

Work-capacity testing in the disabled population is very similar to that in the able-bodied except that the modalities are modified to suit the specific individual's symptoms and/or medical limitations. General cardiovascular endurance exercises can benefit polio survivors, but mechanical stresses to tendons and joints must be minimized. The GXT should be discontinued at the first sign of pain or muscle fatigue.

METHODS

Work-capacity testing of 35 post-polio survivors included 20 females and 15 males between the ages of 32 and 70 years, with an average age of 48.5 years. Whether age at onset was equal to, under, or over 10 years, the number of years post-polio at the time of testing and the years post-polio prior to the onset of new symptoms are presented in Table 1. Thirty-three survivors had

TABLE 1. Relationship of Age to Polio Symptoms

Age	Female Mean (Range)	Male Mean (Range)	Total Mean (Range)
	49 (34–70)	48 (32–69)	48.5 (32–70)
<i>Yrs post-polio</i>	39 (29–68)	39 (27–67)	39 (27–68)
<i>Yrs post-polio to onset new symptoms</i>	36 (20–59)	36 (17–66)	36 (17–66)
<i>N ≤ 10 yrs at onset</i>	13	11	24
<i>N > 10 yrs at onset</i>	7	4	11

new symptoms. Two had come for evaluation because of concern generated by the publicity of post-polio sequelae.

Testing was carried out between October 1979 and February 1986 with the majority of tests in 1985. Clients were categorized into 3 groups (Table 2) according to ambulatory capability. Exercise testing was initiated on selected exercise equipment to ascertain to what degree muscle fatigue limited maximal aerobic work capacity. Our patients were tested on 3 different modalities in the Work Physiology Laboratory depending on their individual suitability: a Monarch arm ergometer, a Quinton treadmill, and a Collins chair ergometer. Exercise was either multistage, interval, or continuous, with continuous exercise utilized in the subjects considered capable of handling it by history and physical examination.

The weights of the subjects were reviewed using tables of desirable weights for men and women aged 25 years and over, prepared by the Metropolitan Life Insurance Company, New York, 1959. The range of ideal body weight was taken to include small, medium, and large frames since the subjects had not been categorized into body frame groups. Arm spans were not measured to give a corrected height in the scoliotic subjects.

RESULTS

According to the broad standards described above, 5 women and 2 men were above ideal body weight (IBW); 6 of them by <5% of the maximum value, but one woman by 40% above. Eight subjects were below IBW. One man was <5% below IBW, 2 women and 4 men were between 9% and 19% below IBW, and one man was 49% below IBW.

Scoliosis was common: 60% of the women and 73% of the men had none-to-mild scoliosis; 40% of the women and 27% of the men had moderate-to-severe scoliosis. Data were taken from the physical examinations; the actual curves were not measured.

The vital capacities (VCs) of the groups, which are not statistically different, are shown in Table 3 ($P = .17$). If arm spans had been used to give a

TABLE 2. Post-Polio Work Capacity

	No. Male	No. Female	Total
I	6	11	17
II	6	5	11
III	3	4	7
N	15	20	35

Group I—ambulatory without restriction to moderate restriction.

Group II—ambulatory with moderately severe to severe restriction.

Group III—wheelchair bound.

corrected height for the scoliotic subjects, the overall results would have been slightly lower. There were 8 ventilator users nights and as needed during the day, 2 in Group I, 4 in Group II, and 2 in Group III. All ventilator users had VCs <50%, and all persons with VCs <50%, with the exception of one male nonsmoker with a VC of 48%, used a ventilator some time during the day. Only 2 persons with “upside down polio” and VCs of 31 and 33%, respectively, fell into Group I. This form of polio involves the upper half of the trunk and the arms to a severe degree and the lower half of the trunk and the legs to a mild degree or not at all. All others in Group I had VCs >55%.

In Group II, 5 persons had VCs <50%. The one man with a VC of 16%, weighed 49% below IBW, had severe scoliosis, and was the only subject who required his ventilator during exercise.

In Group III, the one woman and one man with VCs 48% and 45%, respectively, who were ventilator-dependent, had been smokers and had stopped because of serious pulmonary compromise.

Surprisingly, fully 38% of the 34 subjects for whom data were available showed an obstructed pattern on forced vital capacity. Forty percent of the obstructed group were currently smokers, whereas only 10% of the nonobstructed group were currently smokers. This difference is significant ($P = .05$). The obstructive pattern, seen in all 3 subject groups, was mild-to-moderate in 10 persons and severe in 3. One person showed a fixed extrathoracic type of obstruction, and evaluation by a nose and throat specialist was recommended.

TABLE 3. Vital Capacity of Post-Polio Subjects

Group	No.	Vital Capacity	
		Mean	(SD)
I	16	79.4	(24.3)
II	11	64.6	(30.7)
III	7	60.7	(10.9)

TABLE 4. Resting Oxygen Consumption ($\dot{V}O_2$) of Post-Polio Subjects

Group	No.	$\dot{V}O_2$	
		Mean	(SD)
I	17	3.03	(.75)
II	9	2.68	(.51)
III	6	2.68	(.53)

The resting O_2 consumption ($\dot{V}O_2$) values are presented in Table 4. There is no statistical difference in the values for the 3 groups ($P = .31$). The majority of values were below the arbitrary value of 3.5 ml O_2 /kg/min used in exercise physiology for the calculation of METS (Table 4). For the post-polio survivors during exercise, METS were calculated using both the client's resting $\dot{V}O_2$, and the standard $\dot{V}O_2$ of 3.5. These results are found in Table 5. The results on the hand ergometer are essentially the same for all 3 groups (A, $P = .84$; B, $P = .92$). On the treadmill/chair ergometer, the results appear to be somewhat lower in Group II, but this difference does not reach statistical significance (A, $P = 0.25$; B, $P = .08$). These results reflect the clients' scores on manual muscle tests indicated in Table 6.

To quantitate muscle strength for comparison among the 3 groups, we used a rating system based on that of the Medical Research Council, as discussed by Dalakas et al [1]. Additional weight was given to the muscles of the hips and hands so that the total score became 160, with 40 points assigned to each limb. The rating system is in the Appendix. Complete testing had been done on 16 clients. The number of clients tested in Groups II and III was so small that they were combined in the statistical analysis. In the upper limbs, there is no difference between the scores for Group I and the combined Groups II and III ($P = .15$). In the lower limbs, there is a marked statistical difference between the scores of Group I and the combined Groups II and III ($P = .001$). However, the right combination of functional muscles and bracing allowed clients in Group II to continue limited walking, whereas clients in Group III were wheelchair bound. Like the lower limb scores, the total score for manual

TABLE 5. Post-Polio Energy Expenditure in METS

Group	MET Hand A		MET Hand B		Treadmill/Chair A		Treadmill/Chair B	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
I	3.99	(1.24)	3.15	(1.48)	5.41	(2.3)	4.97	(2.2)
II	4.31	(1.30)	3.27	(.92)	3.95	(1.8)	2.83	(1.4)
III	3.01	(.78)	3.02	(.45)				

A—calculated from client's resting $\dot{V}O_2$

B—calculated from standard $\dot{V}O_2$ —3.5

TABLE 6. Post-Polio Scores on Manual Muscle Tests

Group	No.	Upper Limbs		Lower Limbs		Total Muscle	
		Mean	(SD)	Mean	(SD)	Mean	(SD)
I	9	69.78	(6.9)	64.22	(12.74)	129.89	(17.36)
II, III	7	62.14	(13.1)	32.00	(7.93)	93.86	(10.33)

muscle testing showed a marked statistical difference between Group I and the combined Groups II and III ($P = .001$).

Results of the metabolic and cardiovascular exercise levels attained are reported according to the percentage of maximal heart rate attained (Table 7), double product in terms of multiples of the resting value (Table 8), hand ergometer $\dot{V}O_2$ max, time and watts (Tables 9 and 10); chair ergometer/treadmill $\dot{V}O_2$ max, time (Tables 11 and 12).

The percentage of maximal heart rate attained was taken from the subject's best test, whether it was hand ergometer, chair ergometer, or treadmill. In Table 7 it appears that Group III did not attain as high a value as the other groups, but there is no statistical difference among the groups ($P = 0.32$). All tests in Group III (wheelchair bound) by necessity were carried out on the hand ergometer. Double product is the result of multiplying the maximal heart rate attained by the maximal systolic blood pressure. It is commonly used as an indicator of maximal cardiac output. Two persons in Group II and 2 persons in Group III were on cardiovascular medications that may have affected the double product attained. For the average population the double product during exercise can be increased 3 to 5 times the resting value. For the long-term care hospital population, it has been our experience that the client can only increase the double product by $1\frac{1}{2}$ to 2 times the resting value. The post-polio clients were comparable to or slightly better than a hospital population. There was no statistical difference among the post-polio groups ($P = .22$). Maximal oxygen uptake ($\dot{V}O_2$ max) is not reported in raw values because the results vary with age and sex, and can be divided into low, average, and high normal values. A table adapted from *Exercising Testing and Training of Apparently Healthy Individuals: A Handbook for Physicians*, American Heart Association, 1972 was used in order to rate the $\dot{V}O_2$ max of our subjects. In this table, persons are grouped into decades. The table

TABLE 7. Percentage of Maximal Heart Rate Attained by Post-Polio Subjects

Group	No.	Mean	(SD)
I	17	84.5	(14.9)
II	11	82.6	(14.2)
III	7	74.9	(11.8)

TABLE 8. Exercise Levels Attained by Post-Polio Subjects by Double Product

Group	No.	Double Product	
		Mean	(SD)
I	17	2.35	(0.83)
II	11	1.97	(.54)
III	7	1.89	(.42)

gives maximal oxygen uptake in METS, which were converted back to $\dot{V}O_2$ ml/kg/min for ease of comparison.

For rating the use of the hand ergometer, normal values reported for use of the treadmill/chair ergometer were reduced to one third. With the smaller muscle mass of the upper limbs, maximal work in normals is reported as 116 to 133 watts, whereas in the lower limbs, maximal work is reported as 350 watts. Since the utilization of O_2 is directly proportional to the work output, it was considered reasonable to make a table for the arms that would reflect this difference. There is no published table of normal $\dot{V}O_2$ max for the upper limbs in all age groups.

In Table 9, it is noted that there are no subjects in Group III using the hand ergometer who reached a high normal $\dot{V}O_2$ max. Although the time on the hand ergometer was not statistically different in the 3 groups ($P = .63$), in Group III, there were no persons with a time above 9 min, whereas 3 persons in Group I and II were able to work for longer than 9 min. Nor was the work output in terms of watts statistically different among the 3 groups ($P = .10$). $\dot{V}O_2$ max on the treadmill/chair of Group I was average or less, and in Group II the 4 subjects who were able to use the treadmill had a low normal $\dot{V}O_2$ max. Time on the treadmill/chair for Group II was statistically less than that for Group I, averaging about one third as much time ($P = .006$).

In the overwhelming majority (33/35 persons), factors leading to termination of testing were generalized fatigue and/or focal fatigue in the limbs being tested. In Group I, 2 persons also complained of pain in the low back, one person of pain in the low back and legs, one of pain in a scoliotic back, one of shortness of breath, and one of pain in the exercising right arm

TABLE 9. Exercise Levels ($\dot{V}O_2$ max)* Attained by Post-Polio Subjects and Measured by Hand Ergometer

Group	Low	Low-Aver	Aver	Aver-High	High	No.
I	1	3	3	1	4	12
II	—	—	2	2	4	8
III	—	1	1	4	—	6
						26

*Normal taken as $\frac{1}{3}$ $\dot{V}O_2$ max for lower limbs.

TABLE 10. Exercise Levels Attained by Post-Polio Subjects as Measured by Hand Ergometer in Time and Watts

Group	No.	Hand Time		Hand Watt	
		Mean	(SD)	Mean	(SD)
I	12	6.91	(3.2)	32.9	(17.5)
II	8	5.50	(3.9)	26.9	(16.9)
III	7	6.57	(2.0)	15.7	(12.4)

and shoulder. One person stopped walking on the treadmill because of extreme lower limb discomfort before the experience of fatigue. In Group II, one person on the chair ergometer complained of anxiety and that sitting caused pain in his scoliosis, while one person had a blood pressure increase to 200/100. One person complained of shortness of breath before the development of fatigue and was terminated. In Group III, there were no additional complaints. There were no cardiovascular symptoms or signs in the clients during exercise testing that warranted cessation of the test except for the elevated blood pressure in one client.

The majority of subjects in all 3 groups were able to reach an anaerobic threshold (Table 13). This is reported in percent of total exercise time. Although it appears to have occurred earlier on the hand ergometer than on the treadmill/chair ergometer, there is no statistical difference ($P = 0.54$). The anaerobic threshold is also expressed in terms of the percent of $\dot{V}O_2$ max that had been reached at the time it occurred. On the average, anaerobic threshold was reached when the patient had attained 80–90% of the $\dot{V}O_2$ max. In Group I, one male failed to reach an anaerobic threshold on the treadmill (R Q remained under 0.9) even though he exercised 13.2 min to a double product of $3.5 \times$ resting and 100% heart rate (HR) max. He walked 5–10 miles/day and the good conditioning of his cardiovascular and lower limb musculature may have been the reason. On the other hand, he reached an anaerobic threshold on the hand ergometer in 25% of total exercise time, using muscles that he did not exercise on such a vigorous and regular basis. He had some muscle groups in the right upper limb that were fair minus, and some muscle groups in both legs that were of fair muscle grade. One female was 40% overweight, worked for 15 min on the treadmill to a double product of only $1.6 \times$ resting and to 75% of HR max, and did not reach anaerobics. She did not reach anaerobics working on the hand ergometer for 6 min either. She

TABLE 11. Exercise Levels of Post-Polio Subjects as Compared to Normal $\dot{V}O_2$ max and Measured by Treadmill/Chair Ergometer

Group	<Low	Low	Low-Aver	Aver	Aver-High	High	No.
I	10	1	4	3	—	—	18
II	4	—	—	—	—	—	4

TABLE 12. Post-Polio Subjects' Time on Treadmill/Chair Ergometer

Group	No.	Treadmill/Chair Ergometer	
		Mean	(SD)
I	16	12.7	(5.4)
II	5	4.6	(3.8)

had not only the complaint of easy fatigue, but also, of spasm in all parts of her body subjected to heavy work. Another female who worked for 15 min on the treadmill, but only increased her double product to 2.0 and reached 95% of her HR max, also had similar complaints. These were the only 2 subjects who complained of spasms. Both of these 2 subjects have scattered muscles in all limbs below a fair grade.

One female who did not reach anaerobics had severe back pain related to repeated surgery for dorsal spinal fusion and was on high doses of narcotics. One female was a night ventilator user and walked on the treadmill for up to 12 min, but reached a double product of only $2.3 \times$ resting and 81% HR max. One female reached anaerobics in 13% of an average exercise on the treadmill, and in 17% on the hand ergometer of an average exercise time. She increased her double product to $1.5 \times$ resting and her heart rate to 55% to 65% HR max. Later it was determined that she had an uncontrolled diabetes with a blood sugar of 300 mg%. One female exercised for only 6 min on the hand ergometer and did not reach anaerobics, whereas she exercised 18 min on the treadmill and reached anaerobics in the 13th min. She reached 84% HR max in both tests.

In Group II, 3 persons did not reach anaerobics in hand cycling. One was a 70-year-old female who worked for 2 min and reached 90% HR max, and a double product of only $1.9 \times$ resting. Her upper limbs were considered good to

TABLE 13. Post-Polio Work Capacity Study: Anaerobic Threshold

Group	No.	Hand % Mean	Total Time (SD)	No.	TM/CH % Mean	Total Time (SD)
I	6	66.0	(26.7)	10	75.0	(23.6)
II	4	49.5	(19.2)	2	75.5	(6.4)
III	4	57.5	(24.2)			

Group	No.	Hand % Mean	VO ₂ max (SD)	No.	TM/CH % Mean	VO ₂ max (SD)
I	6	81.5	(17.8)	10	81.4	(15.2)
II	4	87.2	(10.7)	2	89.0	(1.4)
III	4	87.0	(9.6)			

TM/CH = Treadmill/Chair

normal muscle grades. One 69-year-old male, who had only 36% of his VC, cycled for only 4.5 min and reached only $1.6 \times$ resting double product and 68% HR max. A 55-year-old female cycled for only 2 min, increased her double product $1.7 \times$ resting and reached only 60% HR max. Her upper limbs had good muscle grades, but she experienced fatigue in her right arm. Two subjects did not reach anaerobic threshold on the treadmill/chair ergometer. One 61-year-old female walked on the treadmill for only 3 min to 81% HR max and a double product only $1.8 \times$ resting. She had muscle grades from poor to normal in her legs. She required a walker or a 3-legged cane to walk at a slow pace. A second female, 60 years old, has 28% VC, used a ventilator nights, cycled on the chair for only 1.5 min, and increased her double product $1.5 \times$ resting, but her heart rate rose to 93% HR max.

In Group III, one person did not reach anaerobics on the hand ergometer. She exercised for 8 min, increased her double product $2.0 \times$ resting, and reached 84% HR max. She was a ventilator user at night. She had less than fair musculature in both arms. One male subject who reached anaerobic threshold in 25% of his exercise time of 4 min had nonfunctional scapular muscles except for normal elevators, but good-to-normal muscle grades from the elbows down.

DISCUSSION

The following discussion gives a brief description from recent literature of muscle strength and endurance, spasms, and fatigue, and training in neuromuscular disorders, in relation to the exercise prescription for our subjects.

The 2 major factors in determining muscle strength are neural input and intrinsic muscle properties, primarily mass. Various other factors such as age, sex, disuse, disease, and training act by influencing these 2 major components [2]. On mammalian fast-twitch muscle, disuse has been shown to cause atrophy, prolongation of the twitch, loss in contractile strength per gram of tissue with changes in the sarcoplasmic reticulum, and a decrease in myofibrillar protein [3]. In our subjects, muscle mass had been, and continues to be, lost to a greater or lesser degree by the loss of neural input. Remaining neural input may be faulty.

Overutilization, deficient working habits, intercurrent stress, and fatigue from repetitious daily tasks can further detract from strength and endurance. Studies in the elderly (ages 65–90 years) [4] show that muscle area in the limbs declines and with it, strength. We had only 2 subjects in this age category. Studies in normals have shown that the physical endurance limits of dynamic work with small muscle masses are unequivocally lower than the respective values for work with large muscle masses [5]. This explains not only

the lower $\dot{V}O_2$ max for use of the arms v the legs in normals, as well as our subjects, but also the overall decreased $\dot{V}O_2$ resting and max in our subjects from the pathologic loss of muscle mass.

Only 2 clients actually complained of spasms during exercise. Signs of overt neuropathy are found in the general population in a minority of cases when this occurs [6]. However, since spasms may arise from abnormal excitability of the perikaryon (tetany, multiple sclerosis), and since our subjects had polio, which is known to have affected the perikaryon of surviving anterior horn cells, it is reasonable to consider that the spasms in our subjects were related to this damage.

Muscle fatigue during exercise is a common phenomenon, and considered a self-protective mechanism against damage to the contractile machinery of the muscle [7]. Although causes are still not clearly established, involvement of both electrical and metabolic factors has been demonstrated. Endurance training is considered to increase the intensity and duration of exercise without fatigue by altering muscle energy metabolism and contractile properties. Training has been shown to affect muscle fatigue by reducing the slowing of tension development and the slowing of tension relaxation that occurs with fatigue [8]. Both a transformation of fiber type and a change in ultrastructure of the muscle fiber can occur with training [9]. Even activity-induced motor end-plate proliferation in small animals with training has been demonstrated [10].

Articles have already appeared in the literature in the study of cardiovascular responses to exercise in patients with neuromuscular disease [11]. Because exercise forms the mainstay of rehabilitation of patients with neurologic disorders manifesting as paresis or paralysis, Sahgal and Solomon [12] have summarized the broad range of normal muscle responses to exercise and have put this information in perspective in the light of the various muscle disorders. E. Mäikiä [13] of Finland has written a comprehensive article on the use of physiotherapeutic trials in progressive muscular dystrophy diseases. He comments that decreasing strength has a very complicated relationship to real neuromuscular performance and later on with functional ability or disability. Florence and Hagberg [14] have commented that patients with neuromuscular disease have low levels of cardiovascular fitness, and fatigue rapidly during daily activities. They carried out a study to demonstrate that patients with slowly progressive or nonprogressive neuromuscular disease could complete a 12-week training program without untoward responses and could develop cardiovascular training adaptation. This is a form of general or systemic training as distinguished from specific or local training. Their $\dot{V}O_2$ max increased by $25\% \pm 5\%$ with training, and their relative increase in $\dot{V}O_2$ max did not differ from that of healthy subjects undergoing the same training. The authors commented that patients with different diseases, however, need

not respond uniformly; therefore, each disease must be considered individually.

In the prescription of exercise for our subjects, consideration was given to the optimal training heart rate, the anaerobic threshold [15], the results of the manual muscle test, and the pulmonary function tests. Any repetitive activity that appealed to the subject was suggested to him as a conditioning exercise if it were considered safe. If it caused undue pain or muscle fatigue and a sense of weakness that required several hours or one to 2 days for recovery, the subject was advised to cut back both in intensity and duration to a level that did not cause these side effects. Swimming was most commonly prescribed. If clients wished to purchase an ergometer, which is now readily available commercially for exercise programs for the general public, a prescription was given for use on the arm or chair ergometer or on the treadmill.

Light weight lifting with specified repetitions/minute or arm lifts, laps in the pool, swimming with legs supported in a tube and paddling with the arms, water calisthenics, leg exercises on the floor, brisk walking, stair climbing, jogging, and even a workout on Nautilus equipment were among the prescriptions given our clients. Thus far, they have benefitted both psychologically and physically from a better understanding of their abilities and of how to maintain their remaining functional capacity.

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WORK PHYSIOLOGY GLOSSARY

Anaerobic Threshold

The anaerobic threshold is the work level above which anaerobic metabolism produces a lactic acidemia, the result of insufficient delivery of oxygenated blood to the active muscles. The anaerobic threshold can be determined by noninvasive methods. As the lactic acid is buffered by bicarbonate in the blood, CO₂ is released. This CO₂ is in excess of that from energy metabolism. The increased CO₂ production is accompanied by an increase in minute ventilation. Plotting either the minute ventilation (\dot{V}_E) or the CO₂ production ($\dot{V}CO_2$) inflection point or “break point” indicates the anaerobic threshold.

Ergometer

A device used to measure work. The word is derived from the Greek *ergon* meaning work and *metron* meaning measurement. A reliable ergometer must be easy to calibrate.

Joule (J)

The “modern” measure of work or energy (see CALORIE). 1,000 joule is 1 kilojoule (kJ); 1,000 kJ = 1 megajoule (MJ); 1 kcal = 4.2 kJ.

Calorie

The traditional measure of energy content, eg, in food, and energy output, eg, on man at rest and during various types of physical activities. For each liter of oxygen used, about 5 kilocalories (kcal) are yielded. The energy content of 1 kg of fat (2.2 pounds) is approximately 7,000 kcal. (1 kcal = 1,000 calories). See also JOULE.

Kilopond (Kp)

A measure of force. One Kp is the force acting on the mass of 1 kg (about 2.2 pounds) at normal acceleration of gravity. (See Newton). On the bicycle ergometer, the braking force is set by the adjustment of belt tension.

KPM/MIN (Kilopondmeter per minute)

A measure of rate of work (power) involving a known force and distance. On the bicycle ergometer the force is determined by the brake force setting, and the distance by the pedaling rate (for one complete revolution of one pedal a point on the wheel will move 6.0 m). A person working at a speed of 20 to 25 km/hr with a brake force of 2 kp (20 N) produces an external power of about 600 kpm/min or 100 watt. For an exact measurement of the power, the pace of a metronome or similar pace maker should be used.

Maximal Oxygen Uptake (Maximal aerobic power)

The highest oxygen uptake the individual can attain during heavy dynamic physical exercise while breathing air at sea level. When given in liters/min it reflects the potential of the central circulation; when related to the body weight (ml/(kg × min)) it gives an idea about the potential for prolonged vigorous exercises in which the body is lifted (eg, running).

Newton (N)

The “new” unit for force. One N is the force which gives the mass of 1 kg an acceleration of 1 m/s²; 1 kp = 9.81 N or about 10 N. (Nxm = joule).

Steady State

The volume of oxygen transported from the lungs equals the oxygen need of the tissues. The heart rate should also be maintained on a stable level (± a few beats per minute).

Watt

A measure of power involving a known force and distance (see KMP/MIN). One watt = joule/s = 6.12 kpm/min; 100 watt = approximately 600 kpm/min.

Appendix

<i>Manual muscle test key</i>		Normal	5
		Good plus	4.5
		Good	4
		Good minus	3.8
		Fair plus	3.5
		Fair	3
		Fair minus	2.8
		Poor plus	2.5
		Poor	2
		Poor minus	1.5
		Trace	1
<i>Hip</i>		Flexors	5
		Extensors	5
		Abductors	5
		Adductors	5
<i>Knee</i>		Flexors	5
		Extensors	5
<i>Ankle</i>		Dorsiflexors	5
		Plantar flexors	5
<i>Right LE</i>	40		
<i>Left LE</i>	40		
<i>Subtotal</i>	80		
<i>Shoulder</i>		Flexors	5
		Extensors	5
<i>Elbow</i>		Flexors	5
		Extensors	5
<i>Wrist</i>		Flexors	5
		Extensors	5
<i>Hand (finger)</i>		Flexors	5
		Extensors	5
<i>Right UE</i>	40		
<i>Left UE</i>	40		
<i>Subtotal</i>	80		
<i>TOTAL</i>	160		

Post-Polio Muscle Function

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Most patients who contracted poliomyelitis had a good recovery. They adopted active lives, which included productive vocations and various intensities of avocations. Now, 30 years later, they are experiencing disabling levels of muscle pain, fatigue, and increased weakness. Attempts to regain strength by exercise have tended to increase the symptoms rather than provide relief.

A further concern is that, not infrequently, the symptoms are occurring in the presumably normal, unaffected leg or in the stronger of the 2 limbs when there are known residuals. Manual muscle testing often registers grades 4 and 5 strengths, which seem to be in the range of normal capability. In 1961, however, Beasley [1] identified through quantitative testing that grade 5 was only 75% of normal and grade 4 represented a 40% capability. This finding, combined with the mixture of symptoms and failure to respond to exercise, suggests that the problem may be an overuse syndrome. To explore this possibility, dynamic electromyography (EMG) was used to assess the function of the major lower limb muscles during walking.

METHOD

The indication for testing was a clinical need to better define the patient's pattern of muscle function so that appropriate activity guidelines could be provided. The 19 patients studied included 11 men and 8 women. Their average age was 50 years (range 24 to 83) and the mean post-polio interval was 41 years (range 19 to 61).

Dynamic EMG was used to define the relative intensity and timing of the primary weight-bearing muscles during free and fast walking and instrumented torque testing. The basic sample included 3 hip extensors (lower gluteus maximus, semimembranosus, biceps femoris—long head), the vastus lateralis to represent the quadriceps, and the 2 primary ankle plantar flexors (soleus and gastrocnemius). Two hip abductors, gluteus medius and upper gluteus maximus, also were tested, but are not being reported at this time.

Variation in the patient's paralytic pattern or gait deviations introduced occasional modifications in the basic muscle sample.

Fine wire electrodes ($50\ \mu$ with a 2 mm bared tip) were inserted into each target muscle using Basmajian's single needle technique [2]. Accuracy of insertion was confirmed by mild electrical stimulation. Foot switches were taped to the bottom of each foot to designate the intervals of stance and swing. Knee and ankle motion was recorded with anteriorly oriented parallelogram type electrogoniometers applied to each joint. The EMG and foot switch data were transmitted to the recording equipment by FM-FM telemetry, while a cable was used for electrogoniometer signal transmission.

Following electrode placement and confirmation, baseline resting runs were obtained. Dynamic EMG recordings were made during the standard clinical isometric manual strength tests, walking, and instrumented torque testing.

For the walking data, the subjects traversed a 10 m vinyl tile walkway at 2 rates, free and as fast as possible. These recordings were preceded by a familiarization walk. The starting and stopping segments were excluded by photoelectric cells that delineated the middle 6 m of the walkway for data analysis.

All quantitated strength testing was done isometrically. Hip extensor torque was measured with a tensiometer while the subject lay supine and the hip was flexed 30° . Knee extension strength was measured with the subjects sitting and the trunk stabilized against a backboard inclined 30° . The isokinetic dynamometer (Cybex) set at zero velocity was carefully aligned such that the axis of the lever arm matched the knee joint axis during the test. Resistance was applied at the supramalleolar area of the ankle. Ankle plantar flexion was assessed 2 ways. Isometric strength was determined with a tensiometer. The subjects were seated with the knee flexed 90° and the thigh stabilized. Resistance was applied at the metatarsal heads. The standard clinical test of repeated heel rises also was used. A grade of normal was assigned if the patient could accomplish 20 full-range heel rises. Lesser repetitions were graded accordingly.

All data were stored on a 7-channel tape recorder for future computer quantitation. In addition, the data were printed on light-sensitive paper (Visicorder) for immediate visual inspection. The foot switch signals also were transmitted to the stride analyzer for automatic calculations of the stride characteristics, ie, velocity, cadence, and stride length.

Following testing, the EMG signals were quantitated by full-wave rectification and digitization using 2,500 samples per second. All the functional test data were normalized against the EMG value of the individual manual muscle test (MMT) using equal time intervals. The walking data were calculated for each 2% of the gait cycle. All results were reported as a percent

of the manual muscle test (%MMT) [3]. To display the functional effectiveness of the intensities of muscle action exerted during walking, the EMG data also were scaled by Beasley's relative strength values [1]. These latter data were considered representative of the normal functional equivalent. In this preliminary report, data analysis has been limited to descriptive graphs and phasic quantification. The gait cycle was divided into the 7 dynamic phases according to the foot switch pattern, and the mean intensity of the EMG for each muscle was calculated. Duration of each phase as percent of the gait cycle also was defined. The data were grouped according to the subjects' patterns of disability. Their activity patterns were compared to normal function and to each other for both timing and duration.

RESULTS

Subjectively, the patients fell into 2 groups, asymptomatic and symptomatic. The 3 patients in the asymptomatic group had sought medical advice for ways to avoid the "post-polio syndrome." These patients, called the control group, represented a model of effective polio accommodation to disability against which to compare the performance of the symptomatic subjects. All the other patients were seeking treatment for their increasing disability. This symptomatic population was divided into 3 groups according to their paralytic pattern. Seven were classed as "strong" (ie, similar strength in all muscle groups). Another 7 fell into the "weak calf/strong quadriceps" group, while 2 formed a "weak quadriceps/strong calf" class.

Muscle Strength

Individual muscle grades ranged from zero to normal, though most (76%) were between fair plus (3+) and good (4), 11% were between good plus (4+) and normal (5), while the final 13% were fair (3) to trace (1). The "strong" group had the highest mean grades for each muscle group, with all being between 4-, and 4. Mean strength for all the muscles in the control (asymptomatic) and weak quadriceps groups were similar (3+ to 4) except for the quadriceps muscle (3+ v 1). In the group characterized by a "weak calf," the mean muscle strengths were the lowest except for the quadriceps (4). Their hip extensors ranged between 3 and 4-, while the calf muscles were 2 to 3-.

Among the individual muscles, hip extensor strength was quite similar for the groups, with means ranging between 4-, and 3+. Calf strength ranged between 4-, and 4+ for all but the "weak calf/strong quad" group (2 to 3-). Strength of the quadriceps differed in each group, being highest in the "strong" group (4+), grade 4 in the "weak calf" group, 3+ for the "controls," and 1 in the "weak quad" group (Table 1).

TABLE 1. Manual Muscle Grades

	LGM*	Smem†	BF‡	VL§	Sol	Gast¶
Controls	3+	4	4	3+	4	4
Strong	4—	4—	4—	4+	4	4+
Weak calf	3+	4—	3	4	2	3—
Weak quad	3+	4	4	1	4—	4—

*Lower gluteus maximus

†Semimembranosus

‡Bicep femoris

§Vastus lateralis

||Soleus

¶Gastrocnemius

Stride Characteristics

The free velocities of the 4 groups were very similar, and all were significantly below the normal 80 m/min. The patients' means ranged between 60.3 and 65.5 m/min (Table 2). While their free cadence was not grossly abnormal, all groups had short stride lengths (1.14 to 1.27 m, compared to the normal mean of 1.4 m). Minor differences between the groups were negated by the wide standard deviations in the 2 groups with 7 subjects each.

All groups were able to increase their stride characteristics with a fast effort. Most of the gain, however, was by an increase in cadence. While all showed improvement, only the "control" group attained a stride length greater than that for normal free walking. The subjects in the "weak quadriceps" group registered only a 4% gain in strike length during their attempt to walk fast.

TABLE 2. Stride Characteristics

	Velocity (M/min)	Cadence (Step/min)	Stride Length (Meters)
A. Free			
Controls	65.5 (1.4)	102 (2.9)	1.27 (.05)
Strong	63.8 (15.9)	111 (14.0)	1.14 (.19)
Weak calf	60.3 (11.6)	103 (11.3)	1.15 (.13)
Weak quad	62.1	102	1.20
B. Fast			
Controls	111.5 (8.6)	135 (1.4)	1.65 (.11)
Strong	98.9 (21.0)	137 (28.4)	1.46 (.32)
Weak calf	85.5 (17.7)	129 (16.8)	1.32 (.18)
Weak quad	79.5	122.5	1.25

Electromyography

There was considerable difference in the relative intensities and duration of muscle action among the 4 groups. Except in the areas of major weakness (ie, weak quad or weak calf), the functional equivalents closely approximated normal values.

The asymptomatic patient group (controls) displayed 3 patterns of muscle action. All 3 hip extensors (gluteus maximus and both hamstrings) exhibited vigorous terminal swing activity (31% to 37% MMT) followed by a rapid decline and termination of effort in the loading response (6% to 10% GC). Only the biceps femoris continued its action in midstance and terminal stance and this was at a modest level (8% to 19% MMT) (Fig. 1).

Knee extension was similar. The vastus lateralis showed moderate terminal swing action (29% MMT) followed by intensive loading response activity (74% MMT). This markedly declined in early midstance (18%) but continued intermittently at a low level (11% MMT) throughout the rest of stance.

The calf muscles showed the most intense activity. Beginning in terminal swing with a brief intense contraction (80% MMT), the soleus registered continuous and increasingly intense action (30% to 56% MMT) from initial contact through terminal stance. The gastrocnemius began its action at the onset of midstance and progressively increased the intensity until the end of terminal stance (27% to 44% MMT).

Strong

The hip extensors differed in their action patterns. While all 3 became active in terminal swing and continued into loading response, participation by the biceps femoris was mild (13% MMT). The gluteus maximus contracted at a moderate level in terminal swing (24% MMT), increased slightly during the loading response (37% MMT), and persisted through terminal stance at a low level (13% MMT). Semimembranosus action was the most vigorous and persistent, averaging 53% MMT in terminal swing and loading response, then continuing through stance into preswing at levels of 9% to 31% MMT (Fig. 2).

Quadriceps (VL) action was mild and brief. It started in terminal swing at a low level (7% MMT), increased to 19% in loading response, reduced to 7% in midstance, and then relaxed.

The soleus began with slight activity (11% MMT) at the end of terminal swing. This progressively increased from loading response (27% MMT) through terminal stance (54% MMT). Gastrocnemius action also was premature, beginning in loading response (9% MMT) and increasing to 51% in terminal stance.

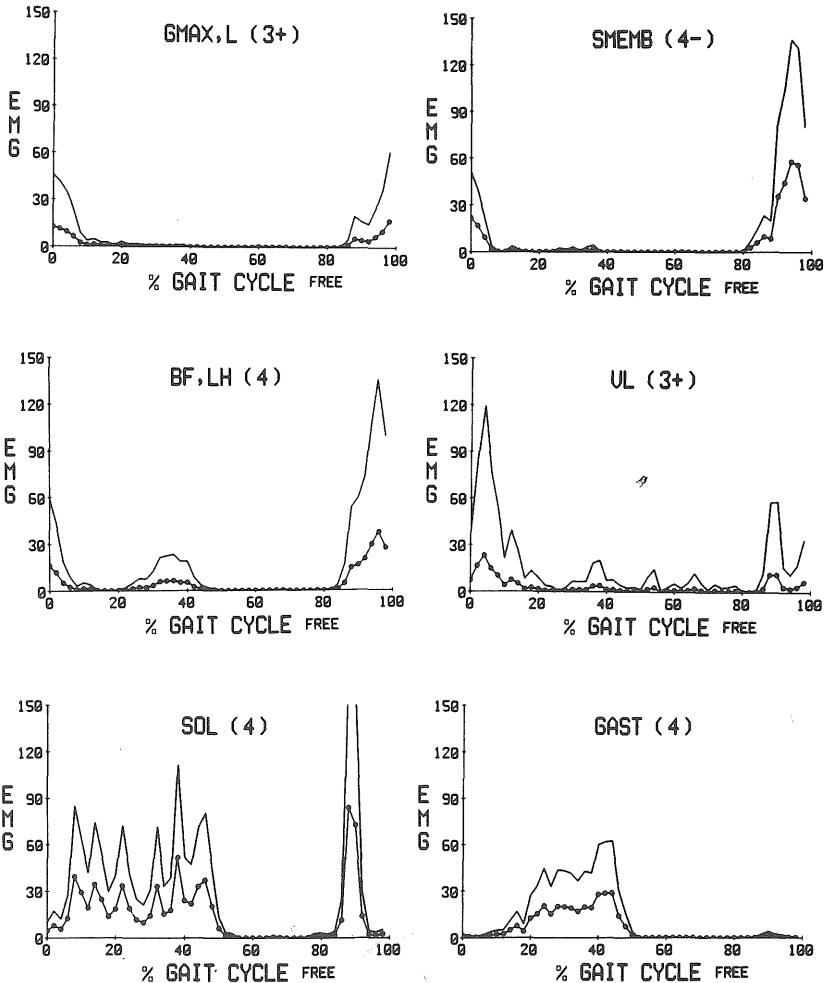


Fig. 1. Asymptomatic Post-Polio Control Group, Dynamic EMG during free walking ($n = 3$). Muscles tested: Lower gluteus maximus (GMAX,L), semimembranosus (SMEMB), biceps femoris, long head (BF,LH), vastus lateralis (VL), soleus (SOL), gastrocnemius (GAST). Manual muscle test grades are shown in parentheses. — — — Normalized, quantitated EMG expressed as a percent of the maximum isometric manual muscle test. —●— Normal equivalent: EMG corrected by Beasley's factor for manual muscle test grade.

Weak Calf/Strong Quadriceps

Muscle activity in these patients was similar to that of the strong group with a few exceptions. Once again, the biceps femoris continued its action into terminal stance, though the intensity dropped from an initial 28% MMT to 11% MMT in the latter phases. The vastus lateralis markedly extended its activity by continuing into initial swing. The intensity of action also was high in both loading response and midstance (51% and 38% MMT). While the calf

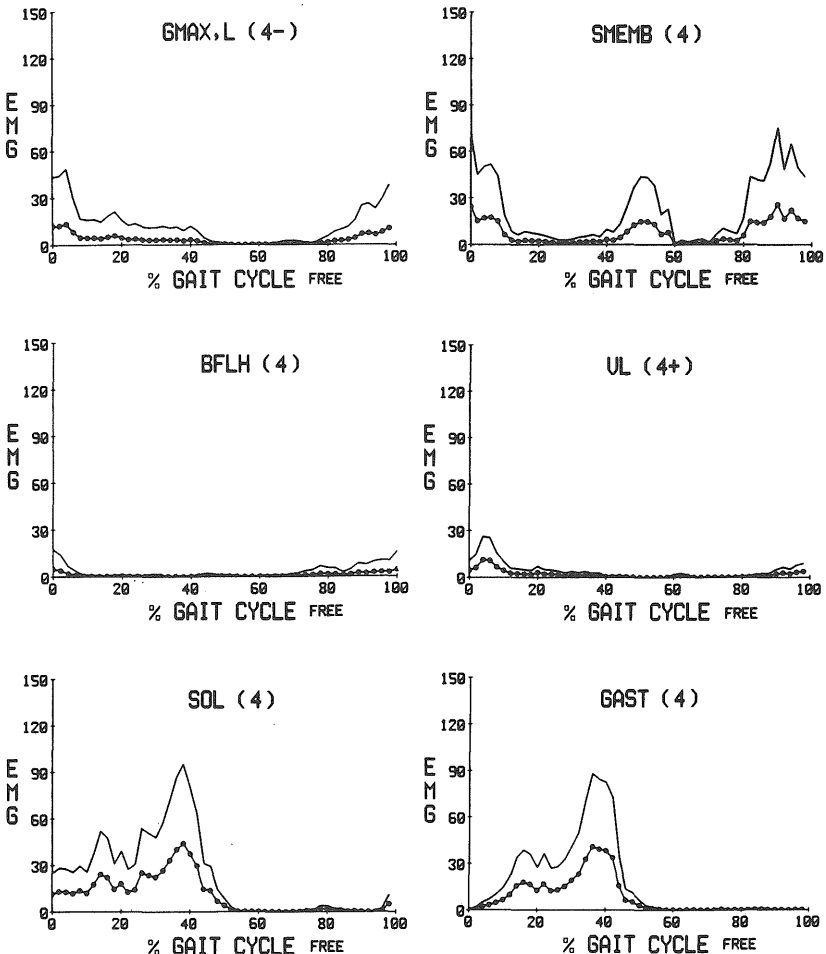


Fig. 2. Symptomatic 'Strong' Post-Polio Group, Dynamic EMG during free walking ($n = 7$). Muscle and data code same as Fig. 1.

muscles were weak, both showed premature onset of swing with persistence and increasing intensity through terminal stance (Fig. 3).

Weak Quadriceps/Strong Calf

There were intense and prolonged efforts to substitute for the weak quadriceps by the gluteus maximus and calf muscles. The gluteus maximus began with vigorous action in terminal swing (85% MMT), continued strong in loading response (64% MMT), and then persisted into terminal stance at a

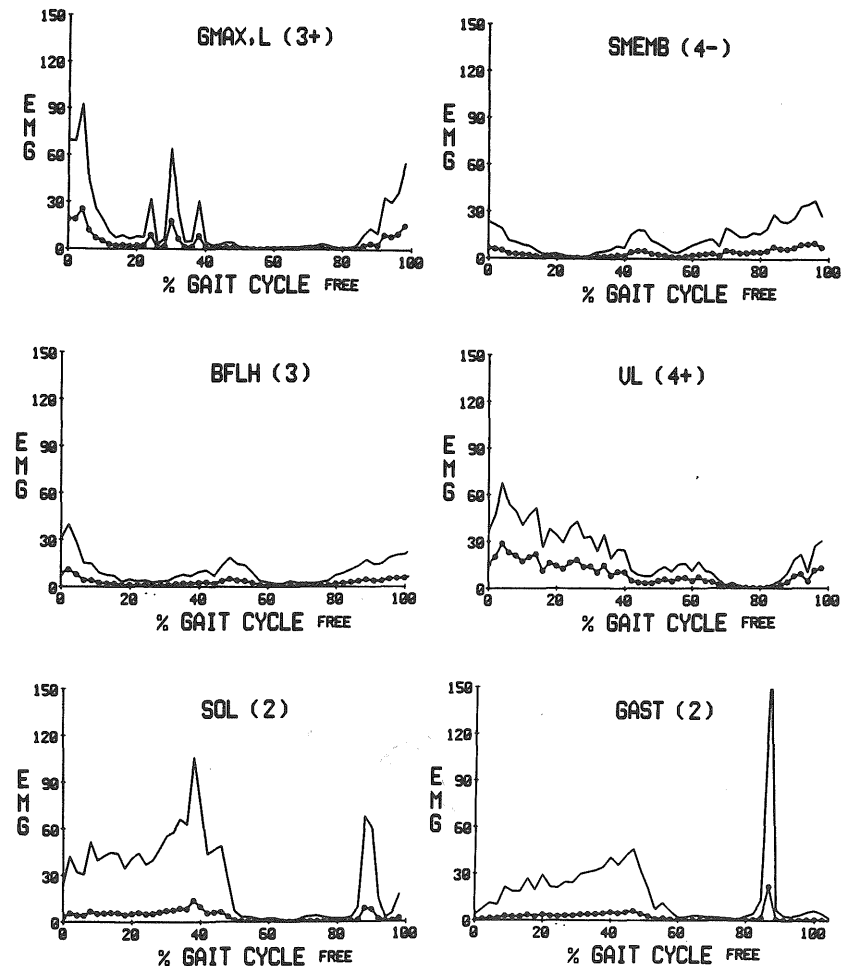


Fig. 3. Symptomatic Weak Calf, Strong Quadriceps Post-Polio Group, Dynamic EMG during free walking (n = 7). Muscle and data code same as Fig. 1.

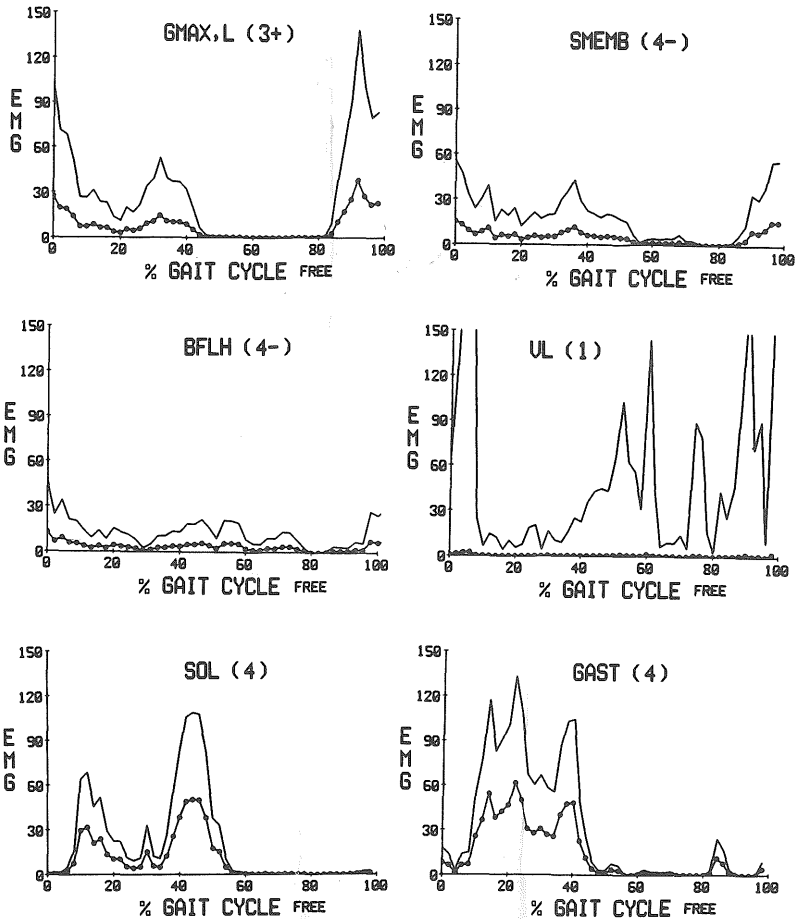


Fig. 4. Symptomatic Weak Quadriceps, Strong Calf Post-Polio Group Dynamic EMG during free walking (n = 2). Muscle and data code same as Fig. 1.

moderate level (32% MMT). Both hamstrings (semimembranosus and biceps femoris) began in terminal swing with moderate action (34% and 39% MMT) and then continued their activity throughout stance and into initial swing. Despite its ineffective strength (trace), the quadriceps (VL) showed intense and persistent action throughout the gait cycle. The levels of activity ranged from 135% MMT in loading response to 11% in initial swing. Among the calf muscles, the gastrocnemius was the more active. Its onset was in swing while the soleus began in loading response. Also, gastrocnemius action was particularly intense in midstance (88% MMT). Both were vigorous in terminal stance (62% and 63% MMT) and both persisted into preswing (Fig. 4).

Normal Equivalents

By Beasley's muscle grade factors, the functional accomplishment of the gluteus maximus was slightly low (5% to 10%) for all groups except those with a weak quadriceps. Semimembranosus effectiveness was high (20%) in terminal swing for both the control and strong groups, and average for the others. Except for terminal swing, the biceps femoris accomplishments tended to be low. Effectiveness of the quadriceps was high in loading response for those with a weak calf, normal for the control group (15%), low in the group called strong (5%), and nonexistent (0%) in the weak quadriceps group. The functional equivalent for the soleus was extremely high for the patients with a weak quadriceps (90%) and very high for the control and strong groups (70% and 60%). Those with a weak calf showed a low accomplishment (15%) in terminal stance. Gastrocnemius effectiveness in each group was similar to that for the soleus but slightly lower (45%, 15%, 30%, 5%, respectively).

Fast Effort

As soon as the patients walked fast, the efficiency of their free gait was lost. Most muscles showed a marked increase in their intensity as well as more frequent prolongation of their activity. These reactions were universal in the quadriceps and very common in both calf muscles. The gluteus maximus showed a notable change only in the groups with either weak quadriceps or calf muscles. Hamstring response was variable. Usually their effort was increased only moderately.

DISCUSSION

Extensor stability is the prime determinant of a person's ability to walk, with optimum function depending on the timely contributions of 4 muscle groups. These are the hamstrings (semimembranosus, biceps femoris long head, semitendinosus), the single joint hip extensors (gluteus maximus, adductor magnus), the quadriceps (4 vasti and the rectus femoris), and the calf muscles (soleus and gastrocnemius). Each muscle group provides a critical function and performs that task in a dominant gait phase between terminal swing and terminal stance. While peak intensity may reach 30% of the maximum isometric muscle test value, mean intensity averages 10% to 15%. Onset and termination of the muscles' actions also blend into the preceding and subsequent phases, thereby providing a smooth transition in limb control. In disabled persons, such as the post-polio, this transition mechanism also facilitates substituting one muscle for another by merely exaggerating an otherwise normal event with premature or prolonged use. Weakness also is augmented by more intense muscle action or reduced performance.

The significance of the post-polio muscle action patterns identified in this study is best understood by considering the events according to the pertinent gait phase. By comparing the reaction of the different clinical groups to normal function, the modes of substitution become evident. Also, relative effectiveness of the different approaches is appreciated.

Terminal swing begins the weight-bearing pattern with preparatory limb positioning. Hamstring deceleration of the thigh reverses hip flexion into an extensor mode. This stabilizes the thigh for active knee extension by the quadriceps (VL). At the same time, the effort is modulated to preserve the hip joint's 30° posture as a compromise between step length and directing the limb toward the ground. Excessive knee hyperextension is avoided by hamstring flexor effect at the knee. Near the end of terminal swing, the gluteus maximus and adductor magnus prepare for their role as primary hip extensors in the next phase.

Among the polio groups, the vigorous action by the hip extensors (gluteus maximus and hamstring muscles) implied the use of rapid deceleration and deliberate hip extension to accentuate knee extension from inertia (past/retract). This was assisted by moderately intense VL action, which was particularly prominent in the weak quadriceps group, where tibial inertia acting opposite an extending thigh was needed as the main knee extensor force. At the same time, the soleus contracted to reduce ankle dorsiflexion and thus lessen the heel lever. Such action minimizes the knee flexion thrust that otherwise would occur with a full heel strike at initial floor contact.

Loading response is a complex phase. Floor contact initiates rapid transfer of body weight onto the limb. The heel strike lever also introduces a knee flexion torque for shock absorption. Peak action of the quadriceps and gluteus maximus (assisted by the adductor magnus) restrains the knee to 15° flexion. At the same time, the hamstrings markedly reduce their action to avoid accentuating knee flexion.

The polio groups used 4 substitutive mechanisms. Knee extension stability was gained by vigorous VL, gluteus maximus and hamstring activity, and premature soleus action. All increased their extensor muscle action sufficiently to assure an effective force (Beasley equivalent). Gluteus maximus effort was twice as great in the 2 groups with specific weakness (calf and quadriceps). Hamstring activity also was maintained at a relatively high level even though some mechanism had to be used to thwart the resulting knee flexion thrust. The knee flexion thrust of a normal heel strike was lessened by premature soleus action to initiate early forefoot contact as well as restrain the advancement of the tibia. This action also would oppose the hamstring knee flexion action.

Midstance begins with the foot flat on the floor and the knee actively stabilized by the quadriceps. As the limb is advancing over the stationary foot, a passive hip extensor force is created, which allows those muscles to relax.

Forward momentum of the body on its single supporting limb begins drawing the ankle toward dorsiflexion. As the tibia approaches vertical, this introduces the threat of increased knee flexion if not controlled. The soleus (assisted by the gastrocnemius) responds. By providing graded plantar flexor forces, the rate of tibial advancement is slowed. This allows the femur to advance relatively faster, and thus passively extend the knee. The quadriceps relaxes as the body weight vector moves anterior to the knee joint center. Subsequent knee stability depends on continued action of the soleus and gastrocnemius.

In all the post-polio groups except the controls, persistence of gluteus maximus and semimembranosus action indicated the need for continued thigh stabilization by the hip extensors during the rest of stance. Except for the weak calf group, which employed a moderately high quadriceps (VL) level of action during midstance, persistent muscle action was at a relatively low intensity. Premature and intense action of the soleus also reduced the quadriceps demand. These substitutions suggest that the manual grades of good to normal for the quadriceps do not reflect existing weakness. At the same time, the calf muscles were exposed to significant overuse.

The knee flexor action of the semimembranosus was counteracted either by soleus action or forward trunk lean in those instances where the VL could reduce its activity.

Terminal stance is the period where the body moves ahead of the supporting foot. Strong soleus and gastrocnemius support of the tibia allows the heel to rise so further step length is gained. This combination of tibial stability and forward trunk alignment also passively stabilizes the knee so the quadriceps can be relaxed. In addition, the upright posture of the trunk introduces relative hip hyperextension, so there is no need for active control at this joint either.

Intense soleus and gastrocnemius activity were the most common post-polio findings, with their functional equivalents also being high in most instances. Activity of one or more hamstrings as well as the gluteus maximus also occurred frequently. Two mechanisms were active. Restraint of tibial advancement to assure knee stability would induce forward lean of the trunk to advance the body. While this posture also contributes to knee stability, it necessitates hip extensor activity to support the trunk. Participation of the hamstrings to assist the gluteus maximus in hip extension is a mixed blessing. Unless the knee is hyperextended, the flexion component of the hamstrings contributes to limb instability. As a result, there must be a functional balance among the multiple substitutive mechanisms. Difficulty in assuring such postural balance with each step may be one of the main contributors to the patients' shortened strides and their correspondingly slower than normal velocities.

The clinical significance of these findings of prolonged and overly intense muscle action in the walking patterns of the post-polio subjects relates to the factors that contribute to physical fatigue and muscle damage. Having sufficient circulation for the muscle to be energized adequately is the critical factor. During continuous effort, the intensity must lie between 15% and 20% of maximum strength to preserve muscle fiber oxygenation [4, 5]. With intermittent activity, a rest interval is assured so greater intensity is tolerated per cycle. The limits still are significant, however. In approximate terms, the duration of the rest (percent of cycle) must exceed the intensity of the muscular effort (percent of maximum strength). Thus, polio efforts of 50% MMT must persist no more than 40% of the gait cycle, a situation that was commonly violated. Fatigue studies of normal persons characteristically display loss of strength when the muscle's endurance is exceeded. This may well relate to the recent studies of phosphocreatine reaction to exhaustive exercise. After the termination of the exercise, 90% was reconstituted in 1 min, but another 20 min were required to regain the last 10% [6].

CONCLUSION

The asymptomatic control group indicates that persons with proper muscle control can accommodate their weakness by an efficient walking pattern. Other persons with seemingly similar patterns of muscular weakness suffer impaired function. The influence of joint deformity needs to be delineated. When this is not a significant deterrent, perhaps gait training by biofeedback technique or selective surgery to alter muscle mechanics can make these persons' gaits more efficient. The final alternative is augmentation of inadequate musculature with orthoses and other walking aids.

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DISCUSSION

DR. WIECHERS: Can we take anything from this into application and the treatment of our patients? Should we insist that they rest more frequently with walking? In other words, when they are tired, are they resting enough on their own or should we recommend that, since their muscles are not getting adequate rest between gait cycles, they should rest more frequently and not push themselves quite so hard with ambulation.

DR. PERRY: Yes, I think that is a good general recommendation.

DR. KOHL: The majority of patients that I work with were taught to tune out pain because that was their first adaptation to the recovery process from the initial onset of polio. Now it appears very important to reteach people to tune into their bodies, to feel the pain, to feel which parts of their bodies and which activities are causing discomfort in order for them to then decide which activities they are going to stop at what duration.

DR. PERRY: The first thing I do is tell the patient that pain is something bad and not something you live with. I try to get people to stay below the pain level, and I have tried to have people not use aspirin to mask pain because that means they are still beating on their muscles.

DR. GOW: The recovery of the fatigue appears also to be the important thing. You can do a lot more work if you do things in short bursts, which is to say 5 to 10 minutes walking and then 5 to 10 minutes recovery and another 5 to 10 minutes walking rather than walking all morning and then taking off all the next afternoon and next day.

DR. PERRY: Oh, absolutely. And that is a very important clinical recommendation to get people to break up their activities and recognize that there is a slow recovery of total fatigue. There is a quick partial recovery but it is incomplete.

Preliminary Observations on Long-Term Muscle Force Changes in the Post-Polio Syndrome*

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Although there is increasing interest in the cause of the post-polio syndrome (PPS), the nature of the clinical problem is still poorly understood. Thus, although the most common patient complaints are progressive weakness and fatigue [1], it has not yet been clearly demonstrated that progressive weakness does indeed occur. Recently, Dalakas et al [2] reported a slow (1%/yr) decline in total body strength in 12 PPS patients. However, the measurement technique used (MRC Scale) is insensitive to even major muscle force changes [3], and thus this conclusion must be viewed cautiously. Other than this study, we are unaware of any attempt to quantify longitudinal change in muscle force in PPS.

We present herein a preliminary report of a prospective, long-term evaluation of muscle force change in patients with PPS.

METHODS

All patients referred to the Neuromuscular Clinic with a suspected diagnosis of PPS were evaluated clinically, electrophysiologically, and with routine blood testing. Patients who met the diagnostic criteria of Dalakas et al [2] were entered into a protocol whereby a Tufts Quantitative Neuromuscular Exam (TQNE) was carried out 3 or 4 times per year. The TQNE is designed to accurately measure voluntary muscle force through maximum voluntary isometric contraction, which we believe is the most direct and valid means of

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assessing motor unit capacity at the present time [4]. The TQNE has an intra- and interrater reliability variance of approximately 8% [4], and has been used to study the natural history of ALS [5] and the results of therapeutic intervention.

To date, 44 patients have been entered into the study. In this communication, we report on the 6 patients who have been followed the longest. These patients have had 5 to 15 TQNEs over a period of 400 to 2,100 days.

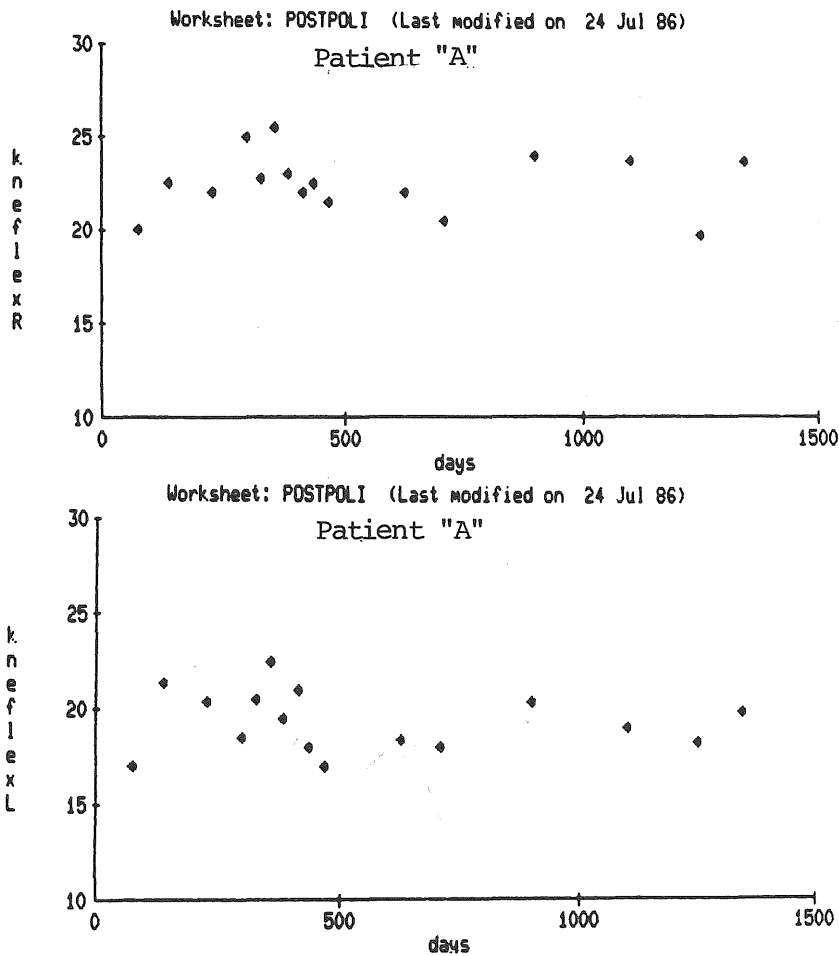


Fig. 1. Arrows in this and subsequent figures indicate sex adjusted mean control value. "O" time indicates 25 days prior to first TQNE. Force values in kilograms. Note seemingly random variance in force over 1400 days in Patient A in both right and left knee flexions.

RESULTS

Examination of time plots of individual muscle groups in the 6 patients revealed no consistent pattern of change. Examples of time plots for selected muscle groups in 3 of these patients are shown in Figures 1-4. Additionally, considerable longitudinal variation in muscle force was observed with seemingly random fluctuations. Of particular interest was the fact that these

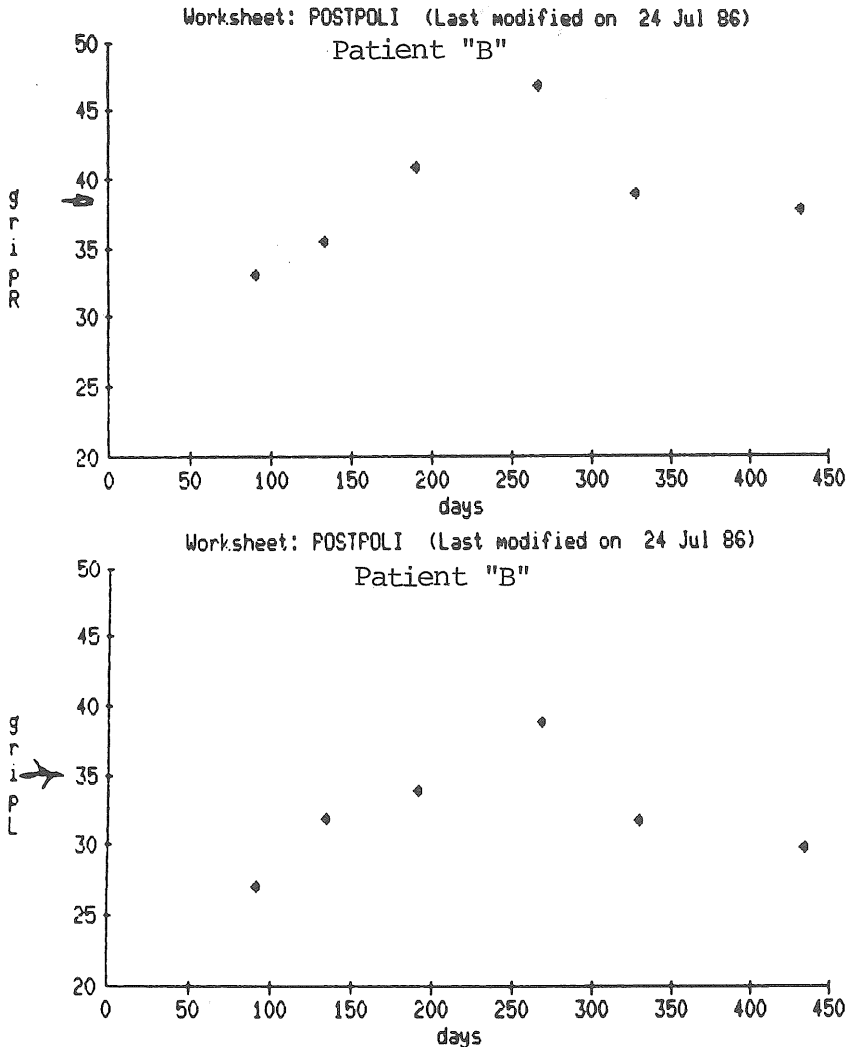
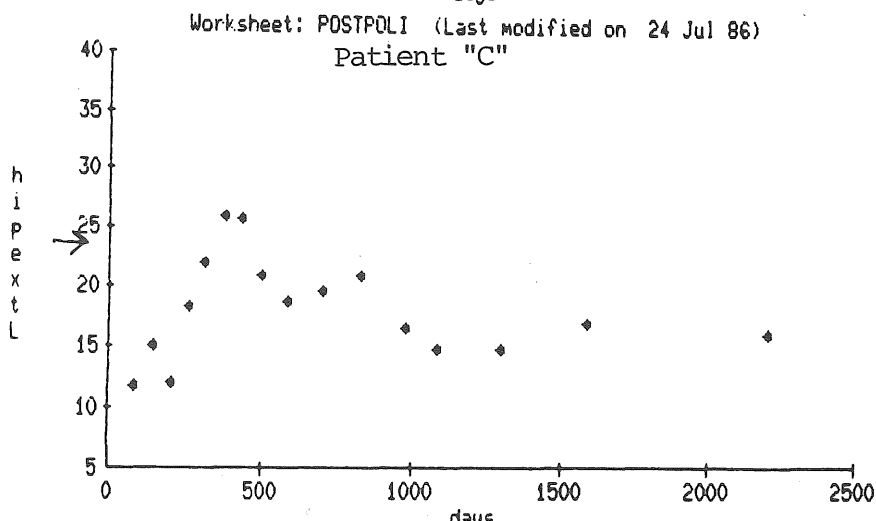
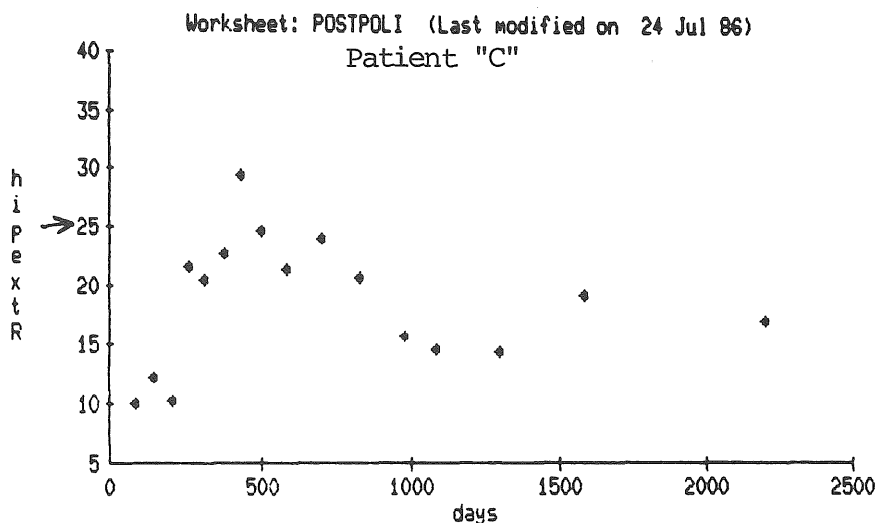


Fig. 2. Patient B demonstrates symmetry of change in right and left grips over 1 year.



Figs. 3 and 4. Five different muscle group forces measured over 2,200 days in *Patient C* strongly suggest concordant change. It is of interest that similar directional changes occur in both strong and weak muscles. "dorsi" = foot dorsiflexion.

fluctuations were usually symmetric (Figs. 2–4) and at times appeared to involve several anatomically separated muscle groups simultaneously (Figs. 3, 4). That is, on the same visit, all muscle groups tended to change in the same direction. We did not observe a pattern of linear decline in force as has been demonstrated in ALS [5].

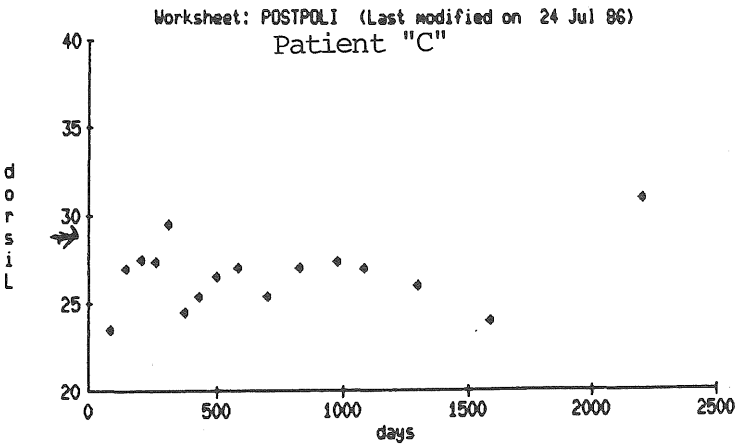
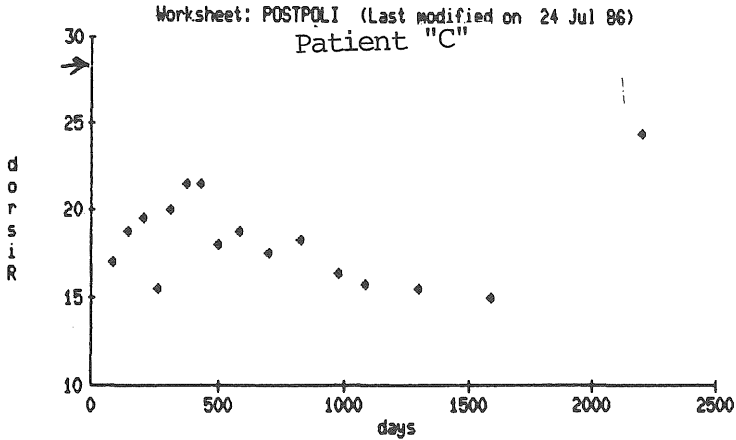
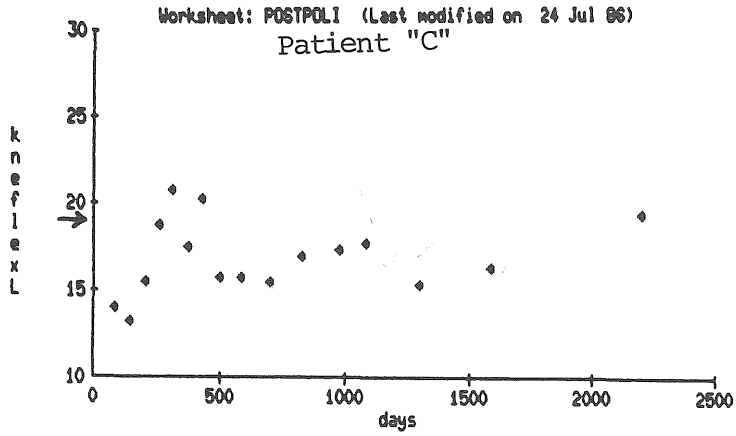


Fig. 4

DISCUSSION

From these very preliminary data in a small number of patients, the most interesting conclusions can be drawn from what was not found. Contrary to what we initially expected on the basis of our clinical judgments, more accurate measurement did not demonstrate a characteristic pattern of muscle force deterioration. Rather, we observed a seemingly random variance of force with time. Although we do not yet have a statistically sound number of longitudinal normal controls, our reliability studies with short-term test-retest [4] suggest that the variance observed in these PPS patients cannot be adequately explained by measurement error. Additionally, studies of maximal isometric voluntary contraction, when carried out by experienced personnel, have demonstrated that variances such as these cannot be attributed to alterations of motivation [6]. Because these fluctuations occurred in the same pattern in most muscle groups, it is doubtful that this represents a random measurement error. Lastly, the fact that these fluctuations in muscle force occurred in a curiously symmetric manner, and often showed similarly directed changes in muscles anatomically at a distance, further suggests that the observed changes are physiologic and meaningful.

Thus, although patients frequently complain of progressive weakness, this could not be substantiated by valid measurements. It appears unlikely that PPS is associated with a progressive loss of motoneurons as is the case in ALS. The seemingly random fluctuations in muscle force suggest a metabolic or possibly immunologic mechanism that operates intermittently to adversely influence motor unit function. This effect may manifest itself more in terms of abnormal fatigability than in atrophy and static weakness.

Our own future studies will involve collecting more normative longitudinal data, increasing our data bank of TQNE information on PPS patients, and exploring abnormal fatigue properties electrophysiologically.

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The Use of Nonfatiguing Strengthening Exercises in Post-Polio Syndrome

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Recognition has increased over the past few years of a new syndrome demonstrated by 25% to 30% of individuals who had acute poliomyelitis during the epidemics of the 1950s [1-3]. Twenty to 30 years after the initial incident, these individuals present with a recurrence of weakness, fatigue, and pain in the same muscle groups that had been paralyzed during the original onset of acute poliomyelitis [4]. Although the reason for this new weakness is different, the same pattern of weakness develops as previously noted during the acute episode. This results in decreased function in many areas, including distance walking, stair climbing and other musculoskeletal functions at home and on the job.

If these patients are subjected to strengthening exercises in physiotherapy without concern for fatigue, instead of improving, they become weakened and ultimately demonstrate atrophy of the affected muscles [5]. If no treatment is performed, function gradually decreases over time as more and more motor units develop deficiencies in function [6, 7].

The cause of this deficit of muscle function is believed to relate to abnormalities that develop in neuromuscular transmission between the terminal axon sprouts, resulting in reinnervation during the recovery phase, and the previously denervated muscle groups that became paralyzed when their corresponding anterior horn cells were destroyed by the polio virus [8, 9]. Weakness with accompanying fatigue results from the inability of this new neuromuscular junction to respond appropriately to demands placed upon it during normal function. As a result, function of motor units decreases within the muscle that demonstrates this more recent weakness.

A pilot project initiated in 1984 demonstrated a beneficial effect of the use of nonfatiguing strengthening exercises in an attempt to at least maintain the level of function of the weakened muscles noted in post-polio syndrome

(PPS). These initial results prompted the development of a research project that is presently underway and is expected to be completed in 1987 [10-12].

MATERIALS AND METHODS

PPS is characterized by weakness in muscles that had been weakened previously by acute poliomyelitis. One of the criteria, therefore, for inclusion in this project was the presence of weakness followed by a period of about 20 years of virtually normal muscle function, which then is followed by a second episode of gradually increasing weakness over the past 3 to 4 years. This weakness is almost always accompanied by fatigue and is frequently associated with muscle and joint pain.

A questionnaire was distributed to patients who thought that they might have PPS. Many of these individuals came to us as a result of publicity in the press relative to the project, as well as a recent post-polio symposium held in Edmonton, Alberta that was widely publicized in the media. Approximately 20% of individuals interviewed and examined were found to have symptoms and signs possibly secondary to PPS [13, 14].

If the questionnaire reflected this pattern of development of muscle weakness, and examination indicated that the muscle weakness was, in fact, present, then electromyography (EMG) was performed on representative muscles demonstrating the weakness as well as other muscles in the same limb that did not have any changes in function. Subjects were admitted into the project only after demonstration of EMG evidence of PPS and a 3-month commitment to attend physiotherapy sessions 3 times weekly.

We have identified EMG changes in what we can now call post-polio muscles as the virtual absence of insertional activity on introduction into, and movement of the needle in, the muscle, combined with the presence of normal-appearing motor unit potentials and a decreased interference pattern when voluntary movement is attempted. This is in contrast with normal muscle or muscle that is weakened as a result of disuse, in which insertional activity is normal and interference pattern is variable. On occasion, we have seen polyphasic potentials present in post-polio muscles. [10-12].

Muscles that had been identified by EMG as being weakened secondary to PPS were subjected to a physiotherapy program of nonfatiguing, strengthening exercises. The starting point for these exercises was arbitrarily chosen as a value of 50% of the weight that could be lifted through 5 repetitions by the particular muscle being treated. For example, if 10 pounds could be lifted through 5 repetitions by the biceps muscle, (which had been identified as having the EMG characteristics of a post-polio muscle), then the exercise program began at 5 pounds through 5 repetitions. The number of repetitions was gradually increased while constantly monitoring for the presence of

fatigue, either during or after the exercise, until a total of 30 repetitions had been achieved. At that point, the weight was increased by an amount easily tolerated by the patient (usually 75% of the initial weight), and this weight was again lifted through the 5 repetitions while gradually increasing the number of repetitions again to 30. This gradual progression of weight and repetitions was continued until a maintenance level was reached, characterized by the presence of fatigue if any further progress were attempted.

It is generally felt that it takes between 3 and 6 months to achieve the maintenance level, and the patient is then asked to continue this maintenance level of exercise for an indefinite period of time.

Each patient was treated in physiotherapy 3 times weekly by the same therapist for the duration of time required.

In addition, another therapist was involved in measuring muscle strength with the use of a myometer. This device measures muscle strength in kilograms and has been shown to be accurate and very reliable if the same person does the testing on the patient each time. We have achieved this by employing a staff therapist who does nothing else to these patients except

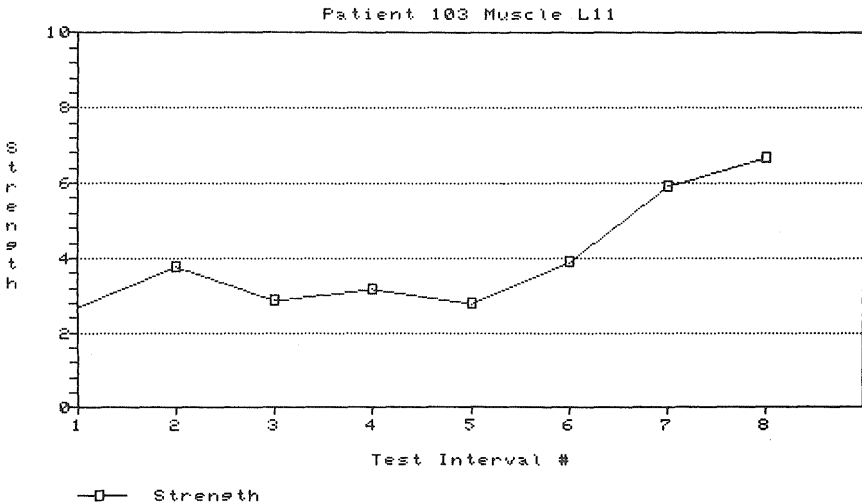


Fig. 1. Patterns of muscle response to nonfatiguing strengthening exercises. Strengthening effect. Note: The interval between measurements on all figures is two weeks. The muscle strength of each patient was measured in units of kilogram (kg) force. Since some of the patients showed smaller changes in their respective post-polio muscles, it was necessary to increase the scale on the Y-axis (strength axis). On the top of the Y-axis is noted (/100) that the scale has been changed. Therefore, graphs that indicate a strength of, for example, 300 and have a /100 on top of the strength axis, actually have a strength of $300/100 = 3$.

measure their patients' muscle strength with the myometer [15]. There is no communication about patients between the 2 physiotherapists assigned to the project.

After establishing a baseline value for each muscle, measurements of muscle strength are performed every 2 weeks. An average of 3 consecutive readings is taken as the final value. An increase in the averaged number value shown on the myometer indicates an increase in muscle strength.

RESULTS

Thirty-two muscles have been treated in 6 patients for an least 24 weeks. Myometer readings indicate that, at the very least, the preexisting level of muscle activity is maintained without any further deterioration. Fourteen muscles improved in strength (Figs. 1 and 2), 17 showed no change in strength (Figs. 3 and 4), and only one muscle demonstrated reduced strength. In this latter case, the patient underwent a rather severe emotional strain and all her levels seemed to reduce, with one muscle remaining permanently weakened. A total of 14 subjects are now on the program, with an upper limit of 20 reached by late 1986 [16, 17]. There was no relationship between the degree of weakness and the amount of improvement in muscle strength after exercise.

When the patients are placed on the maintenance program, they are given strict instructions regarding life-style and the need to avoid fatigue while keeping within the limits imposed upon them by their disability. In this way, they are able to maintain their maintenance level for a long period of

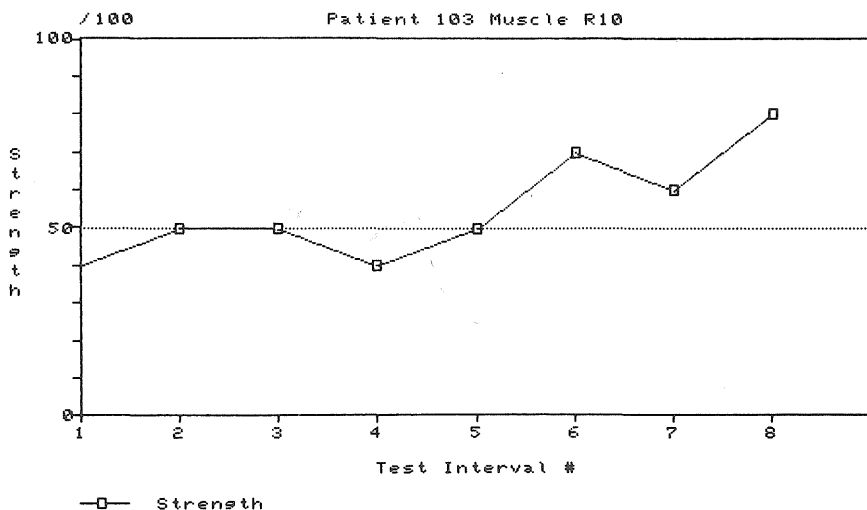


Fig. 2. Patterns of muscle response to nonfatiguing strengthening exercises. Strengthening effect.

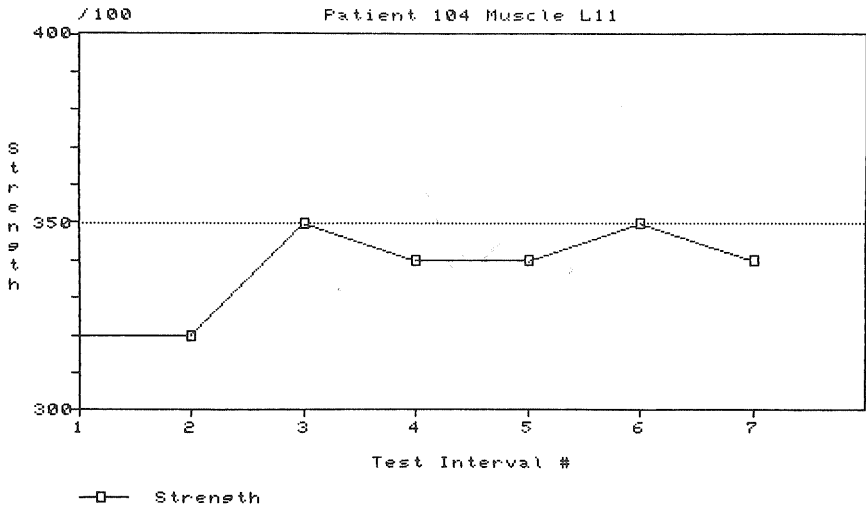


Fig. 3. Patterns of muscle response of nonfatiguing strengthening exercises. Maintenance of pretreatment level.

time. Patients who previously had been on the pilot project portion of this study have maintained their level of function for well over a year, with dips in function taking place whenever they strayed from the instructions that had been given to them. Each time this happened, they were recuperable with intervention of physiotherapy as long as they always avoided fatigue.

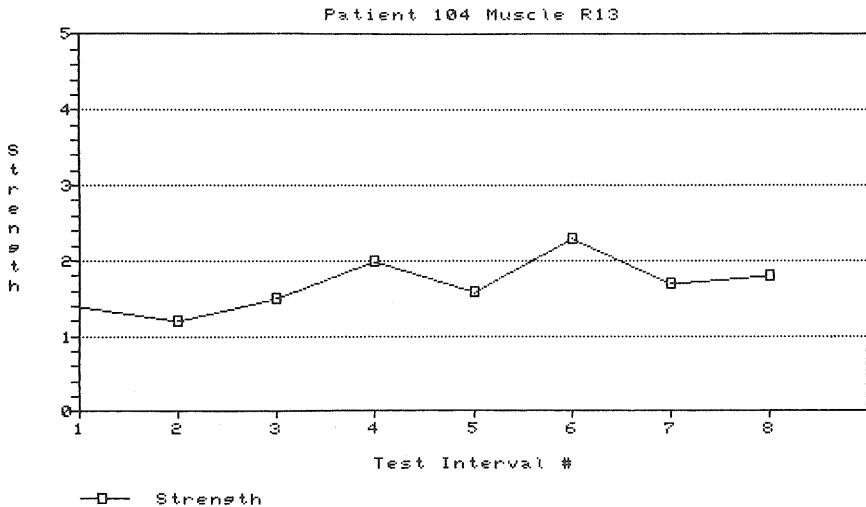


Fig. 4. Patterns of muscle response to nonfatiguing strengthening exercises. Maintenance of pretreatment level.

Thus far, 2 patients have achieved a maintenance level with all affected muscles demonstrating a plateau in strength, after 20 and 24 weeks of treatment, respectively.

SUMMARY

This study has been done to determine if there is any beneficial effect from the use of nonfatiguing strengthening exercises in the presence of post-polio syndrome. Following accurate identification by EMG of muscles that could be called "post-polio muscles," the use of physiotherapy by offering nonfatiguing strengthening exercises provided either a maintenance or a beneficial effect to these muscles. Only one muscle demonstrated reduced strength during the treatment protocol for reasons unassociated with the project. All other muscles, 31 in 6 patients, demonstrated either maintenance of pretreatment strength (17 muscles), or improvement (14 muscles). We feel that the combination of accurate identification of these muscles, followed by strict adherence to a supervised program of nonfatiguing exercise for a period of at least 3 months, provides help for these patients who have developed recurrent weakness 20 years after normal function following poliomyelitis.

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DISCUSSION

DR. SANDERS: I would like to comment. I think we must be careful not to use EMG criteria to define progressive post-polio syndrome unless the results have been confirmed by a blinded comparison with other muscles of similar degree of involvement with the initial disease.

DR. GRIMBY: How did you define that the exercising was not fatiguing?

DR. FELDMAN: Given that post-polio patients are really capable of reporting what they feel by themselves, we use their subjective report of fatigue.

DR. WIECHERS: Is there any way that we can tell early on which muscles are going to make the improvements?

DR. FELDMAN: There is no real relationship that we have been able to find between, for example, the degree of initial weakness and the amount of improvement that might take place. Muscles that really did not improve at all could be determined early by the patient's continued complaint of fatigue with any attempt to increase the exercise.

Clinical Subtypes, DNA Repair Efficiency, and Therapeutic Trials in the Post-Polio Syndromes*

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INTRODUCTION

Acute poliomyelitis was clearly recognized by Charcot and his school by the middle of the 19th century. They were the first to clearly make the separation between acute poliomyelitis and "chronic poliomyelitis," which is now termed amyotrophic lateral sclerosis (ALS) or motor neuron disease. As hygiene improved, polio began to affect older individuals and occur in epidemics. It was the scourge of the first half of the 20th century; major epidemics occurred from the 1930s to the 1950s. Improved medical care during that time led to the survival of many patients, and there are over a quarter million individuals living in the United States who have suffered from paralytic polio [1]. Many of these patients made a complete or considerable recovery despite severe initial paralysis. In the large series of patients reported by Sharrard [2], 45% of muscles with strength of MRC Grade 2 one month after the acute illness, and 80% of those with power of MRC Grade 3 at that time, eventually recovered to MRC Grade 4+ or 5.

However, we are now seeing an increasing number of such patients presenting with progressive problems 30 or 40 years after the acute polio. Cornil and Lépine [3] were the first to report the clinical history and autopsy findings in a patient who developed progressive muscular weakness and wasting many years after an episode of acute polio. Many similar patients have been reported since that time. Zilkha [4] reported a series of 11 patients, 5 of whom had extensor plantar responses, and though he commented on the more benign prognosis of the condition than typical motor neuron disease, he correlated the 2 conditions. Poskanzer et al [5] reviewed 196 ALS patient

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records from the Massachusetts General Hospital, of whom 5 had a definite history of acute poliomyelitis and 2 a possible history. This was calculated to be 9 times the expected frequency of such a history compared with the general population. Unfortunately, the criteria for the diagnosis of ALS were never stated, and it seems likely that patients with a pure lower motor neuron picture and slow progression were wrongly included under the diagnosis of ALS. In their landmark 1972 paper, Mulder et al [6] reviewed their own 34 patients with post-polio syndromes, and concluded their disorder differed from ALS by virtue of the slow progression and predominance of lower motor neuron involvement. Though Mulder et al found abnormal plantar responses in 6 of their 34 cases, none had the typical combination of major upper and lower motor neuron involvement or rapid progression as seen in ALS. Though typical ALS can occur in patients with a previous history of acute polio [7], our experience supports the conclusion of Mulder et al [6]. In our own 20-year series of nearly 150 ALS patients and 20 post-polio patients, only one of the latter had typical ALS.

Recent follow-up surveys of patients who previously suffered paralytic polio had shown a high incidence of late sequelae, ranging from 22% in the regional survey of Olmsted County, Minnesota [8] to over 87% in the national postal survey [9, 10]. The high incidence in the latter survey is clearly due to the method of collecting the data but does indicate the range of symptoms. Several papers in this volume add further information. The extent of deterioration in an individual is very real. In two recent surveys, the proportion of patients using wheelchairs increased by 50%, and the proportion using ventilators increased by 80% to 280% compared with the best level of recovery after the initial polio [10, 11].

The history of polio and the post-polio syndromes is inextricably entwined with ALS and other chronic neurologic degenerations such as Alzheimer and Parkinson diseases. A breakthrough in our understanding of ALS or Alzheimer disease might allow an insight into the post-polio syndromes. Similarly, investigations in the post-polio syndromes may help us understand ALS. Moreover, a drug that is effective in inhibiting the late deterioration of patients who suffer from paralytic polio may be effective in ALS, or Alzheimer, or Parkinson disease. This paper describes studies of

TABLE 1. Post-Polio Syndromes

1) Fatigue
2) Progressive musculoskeletal deformities
3) Pain due to demonstrable causes
4) Pain syndromes without demonstrable cause
5) Progressive post-polio muscular atrophy (PPMA)

DNA repair efficiency in patients with the post-polio syndromes, comparing this with ALS and Alzheimer disease. It also describes a therapeutic trial of purified brain gangliosides (Cronassial, from Fidia Pharmaceutical) in progressive post-polio muscular atrophy (PPMA), comparing the studies with a series of ALS patients.

CLINICAL SUBTYPES OF POST-POLIO SYNDROMES

From surveys in the literature [8–10], and from our own patients' descriptions, it is possible to separate 5 different groups of symptoms in the post-polio syndromes (Tables 1 and 2). Fatigue appears to be the most common late sequela, occurring in 60% to 90% of those with post-polio syndromes. The fatigue appears to be the type commonly encountered in aging patients and those with chronic illnesses such as infections, collagen-vascular diseases, and neoplasms. Progressive increase in skeletal deformities, such as increasing "back knee" deformity, occurs in 25% to 75% of patients in the various surveys. The pain syndromes occur in 50% to 90% of patients, and the surveys variously characterize these as joint or muscle pains. Progressive muscular weakness occurs in 60% to 90% of such patients, usually in previously affected muscles, but also to a lesser extent in historically unaffected muscles.

From the outset, it must be recognized that separating patients into these groups with confidence is difficult, and much further study is needed. Several papers in this volume have added new information in this area. Patients often have 2 or 3 of the features, such as fatigue, muscle pain, and progressive muscular weakness. Moreover, fatigue may cause muscle pain when the patient tries to undertake strong or sustained muscle contraction. Progressive muscle weakness will cause increasing skeletal deformity and pain. Increased skeletal deformity may alter muscle mechanics and produce muscle weakness.

The pain syndromes can be divided into those with a clear etiology, such as a disk prolapse or nerve entrapment, and those where all investigations fail to reveal a cause. Thus, *Patient 8* (Table 2) had an apparently mild attack of poliomyelitis affecting the left leg at the age of 5, and at the age of 26 began having chronic pain in the left buttock and leg area. Spinal x rays showed no significant abnormality (Fig. 1), but CT scan showed extensive atrophy of the paraspinal muscles on the left (Fig. 2). Myelography and electromyography, however, showed no abnormality except for chronic denervation in several of the muscles of the left leg and fibrillation potentials restricted to the L- $\frac{3}{4}$ paraspinal muscles. The etiology of the pain in this patient's condition remains unresolved.

TABLE 2. Clinical Details of Cases in the Study

Subtype	Case No.	Age at			Interval		
		Study/Sex	Polio	Post-Polio Syndrome	Polio to PPS	Polio to Study	PPS to Study
PPMA	1	60/F	24	53	29	36	7
	2	35/M	3	33	30	32	2
	3	75/F	6	74	68	69	1
	4	54/F	25	44	19	29	10
	5	38/M	5	17	12	33	21
Pain Syndrome	6	42/F	7	37	30	35	5
	7	45/F	7	42	35	38	3
	8	34/F	5	26	21	29	8
	9	48/F	10	48	38	38	0.1
Post-Fracture Muscle Weakness	10	56/F	10	55	45	46	1

PPMA is a disorder in which a secondary increase in muscle weakness develops in muscles previously affected and/or unaffected by polio where no cause, such as skeletal deformity or nerve entrapment, can be found. We should probably adopt strict criteria for the diagnosis of PPMA (Table 3), though we should accept the possibility that all of these post-polio syndromes may eventually be proven to arise from progressive denervation of muscle and its consequent effects.

INVESTIGATIONS OF THE ETIOLOGY OF THE POST-POLIO SYNDROMES

Several possible causes of the post-polio syndrome have been proposed over the years. Reactivation of the polio virus, premature aging of chronically overworked anterior horn cells, and secondary degeneration of overworked muscles will be considered.

Reactivated Polio Virus

Intensive search for evidence of reactivation of the polio virus has been as unsuccessful in PPMA as it has been in ALS [12]. However, the findings by Pezeshkpour (this volume) of inflammation in the spinal cords of patients dying many years after acute polio again raise the possibility of continuing activity of the poliovirus in such patients.

TABLE 2. (continued)

	Main Features		EMG—Acute Denervation at Study	Study
	Original Polio	Post-Polio Syndrome		
#1	<i>R leg, L leg, R arm, abdomen, bladder control</i>	<i>Progressive weakness legs, fatigue</i>	+	b
#2	<i>Trunk, R leg</i>	<i>R leg weakness</i>	+	b
#3	<i>L arm</i>	<i>L arm weakness</i>	— (c)	a
#4	<i>Bulbar, both arms</i>	<i>Fatigue, L arm weakness, pain L arm & R leg</i>	+	
#5	<i>L arm, R leg, R arm</i>	<i>Both legs & R arm weakness</i>	+	a
#6	<i>Both legs</i>	<i>Pain both hips & legs</i>	—	
#7	<i>L arm and leg, R foot</i>	<i>Pain L leg, fatigue</i>	—	a
#8	<i>L leg</i>	<i>Pain L leg, fatigue</i>	+	a
#9	<i>Both legs, L arm</i>	<i>Pain both legs, slightly increased weakness, fatigue</i>	—	a
#10	<i>Both legs</i>	<i>L leg weakness, severely worse after fracture L ankle</i>	—	a

a—included in DNA repair study

b—included in ganglioside therapeutic trial

c—no detectable muscle activity in totally paralyzed L arm

Premature Aging

A number of studies have produced evidence of late deterioration of lower motor neurons in patients who have previously suffered paralytic polio. Wiechers and Hubbell [13] performed single fiber EMG (SFEMG) on 10 patients who had suffered from paralytic polio 24 to 60 years previously but who had no complaints of progressive muscle weakness. Eight had abnormally increased jitter in more than 50% of the recordings, and 6 had neuromuscular blocking in more than 30% of recordings. Both abnormalities did not seem to occur until 20 years after acute polio, and to increase with time after the polio. There were positive sharp waves and fibrillation potentials in only 2 of these patients. The blocking and instability of motor unit potentials might explain the fatigue from which these patients suffer, and represent presumably the electrophysiologic counterpart of immature nerve sprouts (thin nerve fibers) seen many years after acute polio [14].

Motor neurons innervating muscles that have recovered from polio have markedly increased motor unit ratios as indicated by giant motor unit potentials and an increase in the maximum macro-EMG motor unit amplitude of up to 40 times the mean normal value [15]. All neurons, both large and small, have a large content of Nissl substance, which indicates that they have a high rate of protein synthesis. An increased motor unit ratio indicates that



Fig. 1. AP x ray of lumbosacral spine of *Patient 8* with the post-polio pain syndrome showing no significant abnormality.

the motor neuron has a markedly increased volume of axoplasm, and hence, the motor neuron has to synthesize a markedly increased amount of protein. This increased protein synthesis implies an increased number of episodes of transcription of the DNA to mRNA, and translation of the mRNA to protein. This increased transcription and translation might be responsible for the premature "wearing out" of the perikaryon, that is, for premature aging. The mechanism for this premature aging might be that the DNA of a postmitotic neuron is incapable of undergoing more than a fixed number of episodes of transcription. There is analogous evidence that mitotic cells, like fibroblasts, are incapable of more than a maximum number of cell divisions (the Hayflick number [16]). Perhaps an increase in the motor unit ratio following polio



Fig. 2. CT scan at L-5 of *Patient 8* showing severe atrophy of the left paraspinous muscles.

causes many motor neurons eventually to exceed the maximum possible number of transcriptional events and hence to die.

An alternative explanation for PPMA is that normal aging begins to affect the few remaining motor neurons. Kawamura et al [17] reported a progressive decrease in the number of spinal motor neurons with age, though in a larger study, Tomlinson and Irving [18] found that this loss did not occur until after the age of 60.

Secondary Degeneration

For many years, it has been known that muscle fiber degeneration occurs in chronic denervating conditions. The evidence for this includes an increased

TABLE 3. Suggested Criteria for Definite Progressive Post-Polio Muscular Atrophy

- 1) History and documented progression of decreased muscle strength
- 2) Past history of acute polio
- 3) Examination showing muscle weakness and/or atrophy in an asymmetric distribution compatible with previous polio
- 4) Electrophysiologic changes of acute denervation superimposed on chronic denervation-reinnervation
- 5) No other etiology demonstrated for progressive weakness

serum creatine kinase and pathologic evidence of necrotic muscle fibers in biopsies from patients with juvenile and adult-onset spinal muscular atrophy and ALS. Drachman et al [19] performed one of the early studies of muscle biopsies from patients with post-polio syndromes and found evidence of muscle fiber degeneration and inflammatory cell infiltration. Dalakas and colleagues [12, 20], who performed a similar survey, emphasized immunologic abnormalities in T-cell subsets and the cerebrospinal fluid (CSF). Further evidence on this point appears elsewhere in this volume (M.C. Dalakas).

One problem with pathologic studies of muscle in the post-polio syndrome is that the changes are patchy, and no accurate quantitative analysis of the changes is possible. Another problem is to decide what is primary and what is secondary. Thus, chronic partial denervation in animals can cause myopathic changes [21] and perhaps even immunologic changes. Our own experience of approximately 15 muscle biopsies from relatively mildly affected muscles of patients with post-polio syndromes has predominantly shown the changes of chronic denervation with secondary myopathic changes. However in addition, cases with tubular aggregates, central cores, and granulovacuolar degeneration have been encountered, and the significance of these changes is uncertain. This problem is likely to be answered only by an extensive serial study of relatively mildly affected muscles in about 100 patients from the earliest possible time after acute polio, documenting muscle strength, quantitative electrophysiologic data including motor unit counts, SFEMG and macro EMG, needle biopsies, and immunologic status.

DNA REPAIR STUDIES IN POST-POLIO SYNDROMES, ALS, AND ALZHEIMER DISEASE

The importance of DNA to the normal functioning of motor neurons has been mentioned above. There is considerable evidence in the literature in human ALS and Alzheimer disease, and in animal models of motor neuron disease, of the presence of structural and functional alterations in nuclear DNA with consequent decrease in RNA and protein synthesis, leading to neuronal death [22–31]. The basis of these abnormalities of nuclear DNA is uncertain, but one possibility to explain the changes in ALS is a defect in a cellular mechanism required for repairing damaged DNA, as suggested by Bradley and Krasin [32, 33].

Defective repair of ultraviolet-induced DNA damage is responsible for xeroderma pigmentosum [34–36], and the extent of the defect has been correlated with the severity of the associated neurologic degeneration [37, 38]. This observation led Robbins and his colleagues [38–41] to hypothesize that DNA repair defects might underly a wide variety of chronic neurologic

diseases. The role of DNA damage and repair in human neurologic and nonneurologic diseases has been reviewed recently [42, 43].

Data from a number of different laboratories, using diverse techniques, support the hypothesis that ALS and Alzheimer disease are due to deficient DNA repair mechanisms [39, 44–51].

We have recently reported studies comparing DNA repair capacity in skin fibroblasts from sporadic ALS patients and controls [52]. We found a statistically significant reduction in cell survival at 72 hours after one hour exposure to an alkylating agent, methyl methane sulfonate (MMS). We also used an assay of unscheduled DNA synthesis, in which the amount of repair occurring after one hour exposure to MMS was measured by the uptake of tritiated thymidine into DNA in the next 4 hours. In ALS fibroblasts, there was a statistically significant reduction in the amount of unscheduled DNA synthesis compared with control fibroblasts. With both of these assays, there was no difference between ALS and control fibroblasts in their response to the DNA cross-linking agent, mitomycin-C, and to x-irradiation or ultraviolet light.

In Alzheimer disease skin fibroblasts, our findings were even more striking, with statistically significant reductions in cell survival and unscheduled DNA synthesis compared with control fibroblasts [53]. We used a further technique, alkaline elution, for studying DNA repair kinetics. In this technique, the molecular size of the DNA is determined at high pH by filtration through a molecular sieve. Exposure of DNA to an alkylating agent produces a number of changes, including alkali-labile apurinic and apyrimidinic sites, which result in single-strand breaks at the high pH. This leads to a reduction in the average molecular size of the DNA, and hence faster elution from the molecular sieve. If normal cells are incubated for 3 hours after a one hour exposure to MMS, they normally repair almost all of the DNA damage, returning the average molecular size to normal. In Alzheimer disease skin fibroblasts, we found a significant reduction in the percent of repair that had occurred by 3 hours after exposure to MMS.

These studies of ALS and Alzheimer disease raise the possibility that PPMA and perhaps other post-polio syndromes arise in patients who are at risk of developing motor neuron degeneration due to an inherently lower than normal DNA repair efficiency. We have investigated this possibility by studying DNA repair in a series of post-polio patients. Skin fibroblast growth is tediously slow; thus, we have developed techniques to study DNA repair by the alkaline elution technique in peripheral blood T-lymphocytes (TLy), which grow much more rapidly [54]. Using these techniques, we have studied repair of DNA damage produced by 50 μ M MMS in TLy of patients with various post-polio syndromes (Table 2). These results in the 6 post-polio patients studied to date are shown in Table 4. Patients with the post-polio

TABLE 4. DNA Repair Efficiency in Peripheral Blood T-Lymphocytes Damaged by 50 μ M MMS (Mean + SEM)

Patient Group	Number	Strand Break Factor		% Recovery at 3 Hr
		0 Hour	3 Hour	
Control	6	0.96 \pm 0.10	0.18 \pm 0.05	80.7 \pm 4.9
Sporadic Alzheimer	2	1.4	0.81	44.6
ALS-				
-familial	6	1.41 \pm 0.13	0.45 \pm 0.03	69.2 \pm 4.9
-sporadic	2	1.17	0.48	65.5
Post-polio syndromes	6	1.37 \pm 0.25	0.33 \pm 0.12	79.1 \pm 3.9

syndromes had normal DNA repair, and differed from patients with ALS and Alzheimer disease. There was no difference between the 2 patients with PPMA and the 4 with other post-polio syndromes in regard to DNA repair. We shall extend these studies, but to date there is no evidence of abnormal DNA repair in patients with post-polio syndromes.

THERAPEUTIC TRIALS OF PURIFIED BRAIN GANGLIOSIDES (CRONASSIAL) IN POST-POLIO SYNDROMES AND ALS

At present, no therapeutic agent has been *proven* to improve human diseases with neuronal and axonal degeneration. However, there are a number of agents that have been suggested to be of value, and we have tested one of these, purified bovine brain gangliosides (Cronassial, Fidia). Gangliosides are complex acidic glycolipids concentrated particularly in neuron cell membranes [55]. They appear to play a role in a number of membrane functions, including excitability [56], enzyme activity [56–58], and receptor function [59]. In the gangliosidoses, there is a dramatic proliferation of neuronal processes, particularly dendrites [60–62]. Gangliosides in vivo and in vitro stimulate innervation of skeletal muscle [63–67] and improve functional recovery after injury of sympathetic [68], peripheral sensory [69], and central neurons [70].

There is evidence that exogenously administered gangliosides are incorporated into nervous tissue [64, 66, 71]. Exogenous gangliosides have been reported to improve neuropathies in experimental animals [72, 73] and in human diabetic and alcoholic neuropathies [74–76].

If a therapeutic agent increases peripheral nerve sprouting, it might slow the rate of deterioration of ALS, peripheral neuropathies, and the post-polio syndromes. In the last 6 years, we have undertaken a number of studies of the therapeutic efficacy of gangliosides in these diseases. In 2 double-blind controlled studies of 40 ALS patients, each studying the effects of daily intramuscular injections of 40 mg of gangliosides for 6 months, neither Bradley et al [77] nor Harrington et al [78] were able to find any significant

benefit from the drug. Though a total of 80 ALS patients were treated, the power of these 2 studies was relatively low. We have recently completed a series of double-blind controlled studies with 40 and 100 mg of intramuscular gangliosides per day in Charcot-Marie-Tooth disease, Friedreich ataxia, and idiopathic polyneuropathy; the results are currently undergoing analysis [79]. Also undertaken was an open study of 100 mg IM daily of gangliosides for 6 months in 2 patients with PPMA (*Patients 1 and 2*, Table 2), and 5 patients with ALS. The patients underwent monthly quantitation of an extensive series of neurologic tests, activities of daily living, muscle strength determinations, and electrophysiologic studies; the patient and a blinded observer also assessed their overall status every month [80–82]. In the analysis of the 2 PPMA patients, 6 test items showed significant deterioration during the drug phase compared with the placebo phase, while 5 test items showed significant improvement. All the remaining items showed no significant change. Similarly, in the 5 ALS patients, the number of items improving and deteriorating balanced one another. It was concluded that there was no evidence of benefit from 100 mg IM daily of gangliosides in either condition.

CONCLUSIONS

A number of apparently different syndromes have been reported in survivors of paralytic polio 20 or more years after the acute illness. The patients can be grouped according to the main symptom: 1) fatigue, 2) progressive skeletal deformity, 3) pain due to demonstrable cause, 4) pain without demonstrable cause, 5) PPMA. However, there is considerable overlap between the groups.

The etiology of these post-polio syndromes has not yet been discovered. Muscle biopsies have shown mild muscle fiber necrosis and inflammatory infiltration, but these and immunologic abnormalities could be secondary to the progressive neuronal degeneration and denervation of the muscle, rather than primary conditions. Single-fiber EMG studies have indicated abnormal peripheral nerve function in asymptomatic post-polio patients 20 to 60 years after the acute illness, and patients with a clear diagnosis of PPMA have EMG evidence of active denervation in muscles that are becoming progressively weaker. It was concluded that the fatigue, progressive skeletal deformities, and PPMA may arise from progressive deterioration of motor neuronal function, which in its final stages causes motor neuron death. There is a need for a serial multidisciplinary study of patients who have previously suffered paralytic polio to help elucidate these questions. A careful autopsy study is also needed.

Studies of the DNA repair efficiency of TLY for the damage produced by an alkylating agent, MMS, indicate that patients with PPMA and other

post-polio syndromes do not differ from normal controls. These findings differ from those in ALS and Alzheimer disease, and indicate that the progressive neuronal degeneration in patients with post-polio syndromes is not due to an inherent defect in DNA repair efficiency for alkylation damage. Possibly the DNA of the postmitotic neuron has a maximum number of transcriptional events it can sustain before degeneration of the process (transcriptional errors) occurs. These lead to impaired motor neuronal metabolism, and hence to nerve terminal and perhaps total neuronal degeneration.

The causes of pain in many of the patients remain a mystery. There is a need for a detailed comparison of the psychologic and other aspects of patients with and without pain. Every patient who has been through paralytic polio has weathered a tremendous psychologic storm, and an understanding of the depth of the psychologic scars may help elucidate the basis of the pain. A detailed autopsy study with neurochemical determination of substance P and other neurotransmitters would also be instructive.

At present, no pharmacologic agent is known to prevent PPMA. Our studies do not indicate that gangliosides are beneficial. Treatment still rests on advice to limit exercise, the provision of orthotic and other rehabilitative devices, stabilizing skeletal deformities, and the treatment of chronic pain with all available pharmacologic and neurobehavioral modalities. An unanswered question concerns the use or dangers of physical therapy and muscle strengthening exercises in patients with the post-polio syndromes.

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DISCUSSION

DR. REA: This is along the line on which we were working with our solvents because they are lipophilic. They create free radicals and they may 1) destroy membranes or 2) they may inhibit repair. Nutritionally you may want to look at the fact that certain vitamins and minerals may have something to do with repair and they may be depleted by the free radicals. We are certainly not sure that the post-polio syndrome has to do with motor neuron degeneration; it may be a vascular phenomenon that is causing the fatigue. I think we have a two-edged sword there, but it still may be regulated metabolically.

DR. BRADLEY: I think that you are absolutely right. The interplay between environmental factors that might be potentially damaging the DNA and the repair mechanism certainly have excited many of us.

DR. MONRO: We have been working on the possibility that there are metabolic deficits in some of our patients that are perhaps genetically induced or perhaps acquired from environmental onslaughts. One of the means that we

have been using is to give people drugs, fairly innocuous drugs, the metabolic pathway of which we know, and then measuring the urinary metabolites of these. If there is a deficit in the urinary metabolites, then we know that the drug hasn't been metabolized. Two of the probes we have used have been to measure self-oxidation and oxidation system cytochrome P450 enzyme oxidase systems. We have found in the majority of people who presented with chemical hypersensitivity and multiple food sensitivities that 80% of them have a self-oxidation deficit and about 20% have a cytochrome P456 enzyme oxidase deficit compared to 20% and 10% in the normal population. It would be quite useful to be able to discern whether this is a problem, particularly in post-polio patients, and I wonder what sort of relevance this has to DNA restoration.

DR BRADLEY: I agree that it is important to find metabolic differences between the post-polio patients and the normal population. That is essentially the line on which we are now working. It is important to have disease controls in the type of experiments you describe. In sick individuals, there are many secondary metabolic changes that could easily influence, for instance, liver function or something of that nature. I need to be convinced that you are not studying such secondary changes.

DR. MULDER: The question I have relates to your hypothesis and how it is compatible with the pathologic studies we saw yesterday from the Armed Forces Institute. Could you comment on that?

DR. BRADLEY: I think that those studies are very exciting because I really believe they open up a totally different line to all of us, a line that at this moment, seems to be outside the metabolic area that I have discussed. I do not think that the two of them have any major relationship. What I have been talking about is what must happen to the nerve cells when there are so few of them and how hard they now have to work. What is going on regarding the inflammation seems to be totally different. We need to define what is occurring virologically in those patients.

DR. GOW: I have a question and a comment. Tissue repair is said to be reduced if you deprive people of their Stage 4 sleep. The question is, does the same thing happen to DNA repair? The comment relates to the behavioral explanation of increased tissue metabolism based on the hypothesis of Walkman and Cooley who view the term dysponesis or misdirected effort that results in heightened arousal of the hypothalamus and the nervous system. This can be detected by excessive action potentials when the patient, in response to real or perceived threat conditions, opens pathways and activates the limbic and autonomic nervous systems so that the nervous system and the musculature are maintained in a state of tension with active metabolism.

When Dr. Mulder was giving an account of the indomitable nature of polio victims to overcome their disability, this revealed to me how these conditioned pathways could have been established at the time of the acute illness with the subsequent reactivation and response that were symptoms of the post-polio syndrome.

DR. BRADLEY: I think the comments that you made with regard to the continuing activation, the continuing drive that patients who have had polio have needed all through their lives and continue to need is undoubtable. There may well be an additional physiologic, that is electrophysiologic, stress on those few remaining nerve cells that is greater than in normal individuals. This bears further study and reemphasis. I have no idea if sleep deprivation alters DNA repair. We assume that the parameters that we are studying here in cells are inherent parameters, not features that are manipulatable by different short-term environmental effects such as sleep deprivation. By and large, it seems our repeated studies on the same patient show the same levels of those parameters and, therefore, I think they are a character of the individual and not altered by short-term environmental effects.

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