LATE EFFECTS OF POLIOMYELITIS

FROM THE FIRST ANNUAL

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on the
LATE EFFECTS OF POLIOMYELITIS

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Foreword

In recent years, increasing numbers of post-polio patients have been showing up in doctors' offices all over the world complaining of a variety of symptoms. Their complaints - pain, weakness and fatigue - at first were considered part of the aging process. But as those complaints increased in number and fervor, the medical profession began to take notice. Could it be something more than a psychological response to an accelerated aging process?

In 1983, two young doctors, Lauro Halstead, M.D., Baylor University College of Medicine, and David O. Wiechers, M.D., Ohio State University, approached the Georgia Warm Springs Foundation requesting a grant to sponsor a research symposium on the late effects of poliomyelitis. They wanted to bring together physicians and researchers from all over the world to pool their knowledge concerning this mysterious condition. The symposium would be held at the Roosevelt Warm Springs Institute for Rehabilitation, Warm Springs, Georgia, where my father, Franklin D. Roosevelt, founded the first medical facility dedicated solely to the rehabilitation of post-polio patients. That was in 1927, and today the Georgia Warm Springs Foundation has grown into a multi-service rehabilitation facility serving people with all types of disabilities.

My father dedicated much of his life to helping the disadvantaged find fulfillment in life. I'm sure he would have felt it fitting to hold the first annual research symposium in Warm Springs, a mecca for polio patients for so many years. It has been almost thirty years since the polio vaccine was discovered, but today persons afflicted with polio number close to 300,000. As I reflect on my father's later years and his fight to overcome the effects of polio, I wonder if he, too, suffered from these late effects. Certainly, his strength waned in later years.

The Board of Trustees of the Georgia Warm Springs Foun-

dation takes pride in sponsoring the symposium, a major step in solving the unique problems of this population.

I would like to thank Dr. Halstead and Dr. Wiechers for their efforts in organizing the symposium and bringing together such a renowned group of researchers, J. Ellies Moran, Executive Director of the Roosevelt Institute and his staff for hosting the symposium, the RGK Foundation, Austin, Texas, and other contributors who made the symposium a reality.

James Roosevelt, President
Roosevelt Warm Springs Foundation

Preface

During my early career in the field of Physical Medicine and Rehabilitation in the early 1970s, my professors often referred to the "old days" and the way in which they managed polio and its complications. My own understanding of the devastating effects of the disease came much later in 1977, when I faced my first acute case of polio. The patient was an unprotected mother, who had undoubtedly acquired the virus from her son, who had been immunized several weeks earlier. In this case, the debilitating effects of the disorder were quickly overcome by this woman's drive to improve her condition. Such intense determination is seen frequently in polio patients today, most likely because they seem to know that if they work hard, they will improve physically. This contrasts with the studies of patients with stroke or spinal cord injury, who soon learn that regardless of the amount of therapy, most of them will not regain physical function in their damaged or injured areas.

Dr. Halstead's experience with polio occurred some 20 years prior to mine, when he was struck by the disease while traveling in Europe as a college student. His insight into the problems of the disease reflects a depth of understanding that can only come through personal experience. The clinical observations that I made in the late 1970s were a reality in his personal life. The complaints of increased fatigue, progressive weakness and muscle discomfort that I was seeing in some older patients in my practice were the same problems that he himself was experiencing.

We met professionally in Houston, Texas, in December 1982, and the topic of discussion turned quickly to post-polio problems. We recognized then the limited information available about the late effects of polio. We questioned our reactions. Was this simply a group of neurologically compromised individuals facing normal problems of aging, or was there indeed a quantifiable change occurring secondary to polio? As we contacted many of our colleagues throughout the country, we found that many of them

shared our concerns. This series of communications culminated in this symposium bringing together interested clinicians and scientists to address the issues and questions of the late effects of polio. Our purpose was not to conclude with definite answers, but to establish whether or not a significant problem did indeed exist and to stimulate interest in further research. It was our hope that the outcome of the symposium would benefit post-polio patients, but moreover, could also possibly provide greater insight into the aging process and its effects on the neuromuscular system.

There was a real comraderie among the participants, as we soon recognized that our knowledge was quite limited. Was this progression of weakness following recovery from post-polio many years ago a new phenomenon, or part of the aging process in a group of neurologically compromised individuals? Dr. Bodian, a member of the Warm Springs Polio Hall of Fame, made a very profound observation when he said we must rephrase our comments about curing polio. What we have succeeded today in curing is the *infection* of polio, but not the disability of its effects. Dr. Bodian stressed the fact that the anterior horn cells that survived and recovered from the initial infection were no doubt scarred. Dr. Tomlinson from England pointed out that the study of the spinal cord in older individuals revealed a loss of anterior horn cells with natural aging. In my own studies of neuromuscular transmission, I found abnormalities of transmission in the old reinnervated motor units of polio patients. The limits of our knowledge regarding the anatomy and physiology of the neuromuscular system of post-polio were reached rapidly early in the course of the symposium.

From his studies at the National Institutes of Health, Dr. Dalakas described two classes of post-polio patients: those who were slowing down physically from natural aging phenomena and those who seemed to slow down with a more rapid loss of motor function. The latter certainly did not reflect an ALS-type picture, but a definite, slowly progressive deterioration of motor function asymmetrically. Weakness was also noted in muscles that had recovered to normal strength following initial paralysis. None of the patients with progressive weakness to date have demonstrated upper motor neuron signs.

Several sessions of the symposium dealt with our efforts to identify specific complaints and to evaluate possible forms of

management. The use of exercise in the post-polio patient who is getting weaker was discussed at great length. It was rapidly recognized that we were unsure of the effects of exercise, since some studies demonstrated definite improvement, while others demonstrated overwork weakness. The need for exercise protocols and future research was stressed.

The problem of muscle pain probably created the greatest controversy. Were we really describing muscle cramping or simple muscle soreness? Differentiating this complaint from the common "tension and stress myalgia" or fibrositis syndrome of normal nonparalytic patients became a difficult task. The use of exercise, electrical stimulation, physical modalities or sublingual therapy to treat this difficult-to-define complaint led to prolonged discussion without conclusions.

The possibility of a latent effect of the virus producing the symptoms still looms in the background as a possible origin of this problem of progressive weakness. No significant proof, however, currently exists and further studies are definitely indicated.

The use of bracing to compensate for the weakened muscles was addressed at length, with many good points of discussion regarding treatment that we can all use today.

Also playing an important role in the post-polio syndrome are the psychological aspects of long-term disability as well as the midlife problems and changes that most of these patients experience. The relationship of psychological problems to complaints of muscle pain, fatigue and even weakness will require further evaluation in the future.

The symposium concluded with a plan of attack to develop not only local interest groups of post-polio patients, but also research and collaborative studies between many centers. We agreed to meet again, probably in one or two years, to reevaluate further work done since the symposium and to keep all interested parties up to date on possible modes of treatment.

David O. Wiechers, M.D.

Introduction

Poliomyelitis has usually been considered a stable, chronic disease. Following the acute illness and a period of rehabilitation, patients eventually achieved a plateau of neurological and functional recovery that remained essentially stable, more or less indefinitely. For the majority of persons who experienced paralytic polio years ago, this still may be true. However, it now appears that as many as one-fourth of these polio survivors are experiencing new health problems which may be related to their illness three or more decades earlier.

In recent years, many of these post-polio patients have been seeking medical help for a variety of complaints that seem to represent new changes in their neurological and functional status. The most common explanation for the cause of such problems after so many years of stability has been aging. However, many of the people who have been experiencing these changes are not particularly old. While many are in their 50s, 60s and 70s, many others are in their 30s and 40s, and some even in their late 20s. So while aging may play some role, it does not seem to be the only explanation.

Unlike the dramatic epidemics in the 1940s and 1950s, which produced widespread alarm, public attention and financial support, the late effects of polio apparently progress slowly and are just now coming to the attention of the medical profession. Consequently, there has been very little organized activity to provide clinical services, fund basic research or educate the public and medical community. Aside from the sporadic case reports published over the past 100 years describing a type of progressive muscular atrophy that occurs in a small number of patients many years after polio, there have been only a handful of articles in the English medical literature during the past two decades which deal with the long-term sequelae of polio.

Because of this lack of scientific information and the increasing needs expressed by polio survivors around the country, it

seemed timely to organize a multidisciplinary conference of interested researchers and clinicians to deal with the medical problems of this population.

At the most basic level, the goals of this conference were to discuss the existence of these new problems and to clarify how widespread they are in the post-polio population. There is no question that the symposium was successful in achieving these goals and represented a major milestone in bringing the problems of post-polio patients to the attention of the medical and lay communities. Related goals were to clarify (1) what is known about the late effects of polio; (2) what are the most likely causes for new neurological changes in post-polio patients; (3) what are the best forms of management; and (4) what are the major research questions that need to be addressed in the coming years. While all of these goals were not fully realized, a good beginning was made in addressing each of these areas during the course of the symposium.

Scope of the Problem

Based on data from the Center for Disease Control, Atlanta, Georgia, there are an estimated 200,000-250,000 survivors in the United States with paralytic polio. According to a preliminary study from the Mayo Clinic presented at this symposium, approximately 25% of this group may be experiencing new health problems related to their earlier infection with polio. Although comparable data are not presently available for other countries, conference participants reported that large numbers of post-polio individuals with new health problems are being seen in other countries, including Canada, England, Denmark and Sweden. Based on our own survey of polio survivors in the United States, the most common new clinical problems are fatigue, weakness in muscles previously affected and unaffected, muscle pain, joint pain, breathing difficulties and cold intolerance. The most common new functional problems are difficulty climbing stairs, walking, dressing and performing wheelchair transfers. The people who appear at greatest risk for developing these new problems are those who at onset required hospitalization, had paralytic involvement of all four limbs, required a ventilator and were over ten years old.

Taxonomy

While no one questioned the occurrence of new health problems, there was considerable diversity of opinion about what was causing them and what to name them. At one extreme was the position that most of these new problems represent a post-polio syndrome, while at the other was the possibility that these new problems could be totally unrelated to the antecedent experience with polio. As the symposium evolved, however, it became increasingly clear that a variety of medical events occur in the polio population which appear to represent a number of different diagnostic entities that we are now only starting to sort out. Based on discussions during and following the conference, a provisional taxonomy was developed which includes two main groups:

1. Problems probably *unrelated* to the residual sequelae of polio, some of which are reversible or curable, eg, hypothyroidism or congestive heart failure causing increased fatigue and weakness;
2. Problems probably *related* to the residual sequelae of polio. This category has two subgroups:
   a. Those with *known* etiologies, eg, musculoskeletal deformities producing nerve entrapment and causing increased focal weakness;
   b. Those with *unknown* etiologies, eg, post-polio progressive muscular atrophy (PPMA).

Etiology

This taxonomy helps simplify questions of etiology in post-polio patients experiencing new health problems. The first category falls into the province of traditional medicine and, while at times diagnostically challenging, by definition does not represent any new etiologic mysteries. Subgroup 2a is also fairly straightforward for the same reasons. By definition, the remaining problems which constitute 2b pose the major etiologic questions.

Although there was no consensus among the participants concerning the most likely causes for problems in this last group, a number of mechanisms were proposed: (1) an immunologic disorder; (2) a compromise of remaining motor neurons in the

spinal cord by scarring, or from an alteration in the supporting structures of the cord which help maintain normal neuronal integrity; (3) a metabolic "fatigue" dysfunction of remaining motor neurons which originally may have been either totally spared or partially damaged, but have been overworked to compensate for neurons that died; (4) a loss of motor neurons through the normal aging process which is clinically more apparent simply because each remaining neuron innervates a larger number of motor fibers; (5) a transmission abnormality at the neuromuscular junction, possibly associated with altered function of the motor neuron, an abnormality of terminal axon sprouts, a dysfunction of transmitter substance or an abnormality of the motor end plates; and (6) abnormalities of the muscle fibers.

Whatever the underlying cause or causes may be for the problems in both groups in category 2, there appears to be a significant time-related component in that many people report experiencing the onset of new problems roughly 30 to 40 years after the initial episode of polio. Whether this interval represents the limits of excessive wear the musculoskeletal system can tolerate, the limits of overworked motor units, or a combination of these and other factors is presently unknown and requires additional investigation.

Management

With regard to the treatment of the late effects of polio, participants agreed that proper management begins with excluding known diagnostic conditions, whether related to the residual sequelae of polio or not. In those individuals who have no clear-cut cause for their new health problems, opinions were divided concerning the best course of action. While there was general agreement that exercise is desirable, it has produced variable results. Some have benefited from closely supervised, individually tailored exercise programs and even regained some of their lost strength. Whether this represents a reversal of disuse weakness or a reversal of the underlying pathology or perhaps even the stimulation of some compensatory mechanism is not known. However, other patients have reported additional or new weakness after undertaking an exercise program. Such clinical findings point to the need for further research and well-defined, individualized exercise protocols.

In the meantime, it makes sense to maintain a level and intensity of daily activity within the limits of comfort. For those experiencing significant weakness or fatigue, increased rest during the day has often been helpful while others have found it necessary to make major alterations in their lifestyle. Finally, there are many others who have discovered the best way of coping was to resume use of a brace, wheelchair or ventilator, either full- or part-time.

Research Questions

The major research questions identified during the course of the symposium fell into the two broad categories of basic and clinical investigation. A partial list of the research projects proposed by the attendees is included in the panel reports at the end of the proceedings.

Further clarification of the underlying mechanism for the new changes being seen in post-polio patients will help define the types of clinical studies that need to be conducted and the most effective forms of therapy. In the meantime, the major clinical questions concern the role and extent of exercise and activity. Additional epidemiological studies will help illuminate a number of questions relating to the prevalence of the various types of delayed sequelae and antecedent risk factors.

Finally, it was our hope that this symposium would accomplish several other goals besides those already mentioned: (1) both the symposium and published proceedings would begin the task of informing the medical profession, polio survivors and the public at large concerning the possible late effects of polio; (2) the symposium would serve as a stimulus to those in attendence, as well as others, to start polio clinics across the country as well as initiate basic and clinical research projects to answer some of the questions raised at the meeting; and (3) the conference would help stimulate interest on the part of private and public agencies to fund polio-related research and clinical activities.

How well these final goals have been achieved will not be known for some time. However, from the interest and enthusiasm expressed at the symposium, and based on follow-up reports of activities that have occurred since the meeting in May, we feel optimistic that these goals will be realized. One example of the impact of this symposium to shape future action occurred dur-

ing the final hours of the conference when Mr. James Roosevelt, President of the Roosevelt Warm Springs Foundation, and Mr. J. Ellies Moran, Executive Director of the Roosevelt Warm Springs Institute for Rehabilitation, made a commitment on behalf of their organizations to finance and host a second symposium on the late effects of polio within the next 18 to 24 months. We are grateful to them for that commitment and look forward to working with them to realize that goal.

Lauro S. Halstead, M.D.
David O. Wiechers, M.D.

Clinical Presentations

Late Effects of Poliomyelitis: Case Reports

David O. Wiechers, M.D.

Introduction

The following five cases are typical of many patients who have lost functional capabilities 30 to 40 years after recovery from paralytic poliomyelitis. The importance of ruling out common medical reasons for the weakness is emphasized, and the question of post-polio syndrome is addressed.

Case 1

A 47-year-old white man contracted poliomyelitis at age 18. The initial paralysis was most severe in the right arm, with less involvement of the other three extremities. Involvement of the diaphragm necessitated respiratory assistance for three weeks. The patient completed his rehabilitation program four months after the onset of polio and was fully ambulatory except for a right short leg brace, which was discarded several months later. Maximum functional recovery occurred two to three years later, when muscles of both legs were of normal strength. From 1957 to 1962, nine reconstructive surgical procedures were performed on the left hand and the right hand, arm and shoulder. The patient continued, however, to have proximal muscle weakness at grade F or 3/5 in the left arm and essentially only hand function in the right upper extremity.

A physically active man, he climbed mountains of 12,300 feet in 1957 and 17,000 feet in 1968 without ill effects. The patient also played tennis and squash but in 1970 began to notice

David O. Wiechers, M.D., Clinical Assistant Professor, Ohio State University, Columbus, Ohio.

excessive fatigue in his left arm. Approximately three years ago, the patient felt a tingling sensation in the left leg while jogging and subsequently developed frequent paresthesias, even after short walks. Computed tomography (CT) scan of the lumbosacral spine was normal at that time. The patient began a strengthening program for his back and abdominal muscles until six months later when he noted increased weakness in the left foot and ankle. Within the next four months, the patient developed bilateral sciatic pain and perirectal paresthesias and was hospitalized. A repeat CT scan was normal. X-ray indicated a continuing mild scoliosis, and a myelogram revealed a very minimal ventral extradural defect at L5 S1 of questionable significance. Pulmonary studies at this time revealed mild restrictive lung disease.

The patient was subsequently discharged. Continued physical therapy provided some relief of his back symptoms, but he continued to have generalized weakness and fatigue which he attributed to his hospitalization and bed rest. This diminished endurance continued and after one month, the patient began noting leg cramping and fasciculations, most notably in the quadriceps muscles.

At this time, the patient also began to notice a mid-afternoon fatigue phenomenon characterized by generalized headaches, clammy sensations, hot or cold flashes across the forehead, intense generalized fatigue and diminished ability to concentrate. This fatigue phenomenon seemed unrelated to physical activity but was helped by brief rest for 15 to 30 minutes.

This patient's symptoms seem to have become cyclical, with a severe bout for two to four weeks, followed by a period of stabilization for 4 to 12 weeks. Recent manual muscle testing showed mild weakness in the left ankle dorsiflexors. Macroelectromyography of muscle revealed evidence of extensive reinnervation of 90% of the motor units.

Case 2

A 49-year-old white woman sustained poliomyelitis at the age of 2 with paralysis of both lower extremities. She did not require a respirator and underwent a successful course of rehabilitation. At the age of 6, manual muscle testing revealed normal strength in the right leg. Between the ages of 8 and 9,

the patient reportedly walked 1-½ miles to and from school four times a day without difficulty, but states that she was never able to run. During the next five years, the patient underwent a series of surgical procedures to the left lower extremity.

In 1977 she had surgery for recurrent dislocation of the left patella and since that time has had difficulty resuming full functional activities. The patient states that, in retrospect, even at the age of 32 she was having significant problems with fatigue and over the past several years has been having increased difficulty with her good right leg. She also has had hip discomfort for approximately five years and in the past year has been falling one or two times a week. Manual muscle testing approximately eight months ago demonstrated weakness of the right lower extremity that had not been previously documented, with a grade F or 3/5 weakness of the ankle evertors and a grade G or 4/5 weakness of the ankle dorsiflexors and hip flexors.

The patient was prescribed a right plastic ankle foot orthosis and her gait markedly improved. She requires less energy for ambulation and has returned to work full-time. Follow-up over the past several months has shown continued weakness in the affected muscles of the right limb and no return of strength in the ankle dorsiflexors despite use of the brace for ambulation. In electrical studies of the right ankle dorsiflexors, 70% of the motor units sampled showed evidence of longstanding reinnervation.

Case 3

A 27-year-old woman had polio at the age of 9 months. The patient was in an iron lung after the onset of acute poliomyelitis. She walked prior to the onset of polio, but afterwards was not capable of walking until age 3 and only with the aid of braces and crutches. She continued to use crutches and a right leg brace until approximately the age of 15 when, after multiple transfer procedures of various muscles throughout both lower extremities, she was able to walk using only the right leg brace.

The patient currently has two children, ages 8 and 2. She works full time as an office manager in a very stressful, busy office.

The patient states that since the birth of her last child, she has noted progressive fatigue and back discomfort. She has a mild

right thoracic, left lumbar scoliosis with a marked pelvic tilt to the right of approximately 2 inches and wears a shoe lift to level the pelvis. Approximately three years ago, the patient began noting numbness in the toes of the left foot associated with pain and discomfort throughout the leg. She underwent multiple work-ups for radiculopathy, including myelograms, all of which were normal. The patient improved with physical therapy and transcutaneous nerve stimulation (TNS).

Approximately one year ago, the patient began to note a recurrence of discomfort in the left leg and back. Within days of the onset of this discomfort, she encountered several very stressful family problems. The patient's mother was hospitalized, her sister graduated from school and left the country, and her brother was hospitalized for a severe neck injury. At this time, the patient and her husband separated, and she and her two children were forced to move out of the home. Approximately two months later her pain became severe and the entire left foot became numb. The numbness radiated up the side of her legs and did not abate.

Palpation of the musculature revealed exquisite tenderness to the lightest touch, with trigger points noted most markedly on the left side of the body in the trapezius, the gluteus medius, the gluteus maximus, the tensor facilata, the distal attachment of the vastis medialis, the origin of gastrocsoleus and the mid-belly of the anterior tibialis. This muscle soreness was also noted in the same muscles on the right side. Muscle strength on the right side in the most painful muscles was in the range of P or 2/5. The marked muscle soreness at the mid-belly of the right anterior tibialis was especially noteworthy because this muscle had a grade of 0/5.

The patient was treated with a program of progressive stretching exercises of the leg muscles. The patient also changed jobs, leaving a very stressful situation. Since that time, her pain has dramatically improved, and her functional activities have almost returned to their previous levels.

Case 4

This 48-year-old white man suffered acute paralytic poliomyelitis at the age of 12. All four extremities were involved except the left forearm. He did not require respiratory assistance,

although his chest musculature was severely involved. After undergoing a rehabilitation program, he was able to walk again at age 14 with the use of bilateral long leg braces and crutches. Several years later, he underwent two spinal fusions as well as multiple muscle transplant procedures at the wrist and knees. Both ankles were also fused. He was left with the residual effects of severe scoliosis and now walks using canes and long leg braces.

Two years ago, the patient began noting increasing back discomfort. His pain has centered around the left side in the mid-thoracic region at the apex of his thoracic curve. With the exception of a grade G or 4/5 knee extensor on the left, he has had essentially no muscle function in the lower extremities. His upper extremity strength has been a grade G or 4/5 throughout the right side and normal strength on the left side. He has noted no progression of weakness in his arms over the years.

A high-school physics and mathematics teacher, the patient has been deeply involved in school activities. He has noted over the past two years progressive pain in the mid-thoracic region of the back that is made worse by prolonged standing at the blackboard or sitting for long periods. He has had a progressive weight gain of 25 to 30 pounds during the past ten years.

X-rays are suggestive of further compression of the concave side of his scoliosis but to a minimal degree. The patient was treated with two aspirin qid and outpatient physical therapy in the form of ultrasound followed by gravity traction of the most painful areas. Over a period of three to four weeks, he made excellent progress in resolving his back discomfort. He still continues to have back discomfort when standing for long periods; however, the pain is much less severe than before. He feels that continuing to perform gravity traction twice a day is helping him to control his low back discomfort.

Case 5

This 42-year-old white woman suffered acute paralytic poliomyelitis in 1948 at age 6, involving her right arm, spine and left hand. Her legs were not involved. She underwent rehabilitation therapy at the Roosevelt Warm Springs Institute. In the past four years, the patient has returned to college and is seeking a graduate degree.

Approximately one year ago, she began to notice intermit-

tent neck stiffness. Three months ago, she awoke with acute pain in the left shoulder with a sudden loss of strength and the inability to raise the left arm above shoulder height. Her pain continued for three weeks before she was seen in consultation. At that time, Spurlings maneuver was positive on the left side, radiating discomfort down into the left shoulder and upper arm. She had a grade P or 2/5 weakness of the deltoid and a grade F+ or a 3+/5 weakness of the left biceps. Her triceps, wrist flexors and extensors were all within normal limits; however, her hand intrinsic muscles were a grade G or a 4/5. X-ray studies of the cervical spine were essentially within normal limits. Electromyographic studies revealed rare positive sharp waves at C5 and C6 in the paraspinal muscles and in the deltoid, biceps and triceps. Motor units in the triceps were extremely large and reinnervated, while motor units in the deltoid and biceps were of normal size, but with a marked reduction in number on maximum contraction. The patient was diagnosed as having an acute C5 radiculopathy and placed on outpatient cervical traction.

The patient was seen in follow-up three weeks later and had a marked resolution of pain. The radiation of discomfort from the neck down into the arm had stopped. Her muscle strength, however, remained unchanged. The patient was placed on a program of home cervical traction and was seen again eight weeks later. Her pain had essentially resolved and her muscle strength was now normal in the shoulder abductors and biceps. The intrinsic muscles of the hand still remained weak at a grade G or 4/5.

Discussion

These five cases are fairly typical of some of the problems facing post-poliomyelitis patients. But which cases represent a true "post-polio syndrome"? The problem of progressive muscle weakness, as demonstrated by the first two cases, represents a definite and quantifiable increase in weakness over time. The weakness seems to come on gradually and is frequently associated with muscle pain.

In the third case, the patient had more muscle pain than weakness. This pain is actually very similar to the type of muscle pain that is seen in patients with myofascial pain or fibrositis syndrome. The third patient's polio may be merely coinciden-

tal, with the subsequent development of severe fibrositis syndrome or tension stress muscle soreness. It is noteworthy that this patient has been helped by exercise and resolution of major stresses in her life.

Although the patient in case 4 had severe poliomyelitis, he has not noted a progression of weakness. However, with advancing age, he has been having problems with structural changes in the bones of his thoracic, cervical and lumbar spine. He has undergone spinal fusions and, because of an increase in weight, has developed significant low back discomfort. A weight reduction program and simple physical therapy measures were sufficient to resolve his symptoms.

Case 5 represents the occurrence of the common medical problem of radiculopathy in a patient who previously had polio. This patient has also not noted any progression of weakness, and her symptoms associated with radiculopathy were resolved with standard treatment.

When one compares cases like these reported here, there does appear to be a true and progressive onset of weakness in some post-poliomyelitis patients. This progression of weakness does not appear to be related to any secondary neuromuscular disease. Rather, it appears to be related to a progression of weakness in muscles previously weakened by polio as well as in muscles that the patient felt to be of normal strength, but when examined electrically, proved to have been compromised previously by the acute poliomyelitis.

It is these patients who do have true progression of muscle weakness that present the dilemma for the practicing physician. Common medical problems certainly must be ruled out in the evaluation of any older polio patient. With or without progressive weakness, the muscle pain that appears to be present in many of these patients is an area for future research. What is the explanation for the third patient's pain in a muscle that essentially had no active function? Hopefully, further study of this problem will provide specific answers to a complicated diagnostic issue.

Late Effects of Poliomyelitis: A National Survey

Lauro S. Halstead, M.D., David O. Wiechers, M.D. and C. Donald Rossi, M.S.

Introduction

For more than 100 years, it has been recognized that there are late sequelae of polio that occur in some patients many years after the initial illness.[1,2] Although there have been numerous articles describing various changes and a number of hypotheses proposed to explain these changes, the nature and cause of these sequelae are still not well understood. The changes most commonly described have included weakness, muscle atrophy, fasciculations, and preservation of normal sensation ocurring up to 71 years after an acute and usually severe attack of paralytic poliomyelitis.[3,4] In most instances, these cases have been diagnosed as progressive muscular atrophy (PMA), although many other diagnostic terms have been applied, such as chronic anterior poliomyelitis, late motor neuron degeneration and forme fruste amyotrophic lateral sclerosis.[3,5,6] The possibility that PMA might be causally associated with antecedent exposure to polio virus has provoked considerable interest over the years because of the important etiologic and diagnostic implications. However, in a recent excellent review of this problem, it was concluded that the role of a previous infection with polio virus in the etiology of PMA is still equivocal.[7] While this conclusion is

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reassuring to those persons who had polio several decades ago, it does not address another phenomenon which apparently has been observed only in the last few years and has not, to our knowledge, been described in the medical literature. This phenomenon is the unexpectedly common occurrence of fairly severe late effects of polio. The changes described in these persons are qualitatively similar to the earlier reports of PMA. What makes this new phenomenon unusual and perplexing, however, are the marked quantitative differences. From our experience and that of colleagues around the country, thousands of persons appear to be experiencing a variety of fairly serious late changes. By contrast, a review of the world's literature from 1875 to the present reveals somewhat less than 150 cases.

Based on a questionnaire survey of 201 persons with a prior history of acute poliomyelitis, the major clinical features of this phenomenon will be described and those factors most commonly associated with development of late sequelae will be identified.

Methods

A 27-item questionnaire was designed, field-tested and distributed to approximately 500 polio survivors between May and July 1983. The questionnaire focused on three principal areas: (1) the extent of involvement at the time of onset; (2) the extent of involvement and functional status after maximum recovery; and (3) new health problems and changes in functional status since maximum recovery. Maximum recovery was defined as that period when patients felt they had achieved a level of maximum strength and function lasting a number of years. There were additional questions about any treatment that was especially helpful or harmful and questions about other chronic health problems such as heart disease, diabetes and hypertension.

Since there was no readily available, well-defined population at risk, questionnaires were distributed to polio survivor groups which expressed an interest in this study. These groups were in Dayton, Ohio; St. Louis, Missouri; Houston, Texas; and Minneapolis, Minnesota. In addition, respondents were encouraged to share copies of the questionnaire with other polio patients they knew. In this manner, questionnaires were circulated to polio survivors across the country. As a result, we have no way of estimating how many persons actually received the questionnaire

and declined to participate in this study. Although we made an effort to reach persons both with and without new problems, those with new difficulties were more likely to respond.

For some analyses, respondents were divided into two groups: hospitalized and nonhospitalized at onset of polio. The nonhospitalized group provided a provisional control population with which to compare the experience of those more seriously affected at onset.

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 two-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 (e.g., age at onset, hospitalization 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

A total of 221 questionnaires were received by August 31, 1983, the final date for entry into the study. Of these 221, 13 were discarded due to incompleteness, inconsistencies or serious question about the original diagnosis of polio. Another seven were excluded from analysis because the respondent had experienced a significant but unrelated health problem since achieving maximum recovery which altered neuromuscular function of daily activities, such as a stroke. This left 201 questionnaires for analysis.

Characteristics of Respondents

The principal characteristics of the 201 respondents are summarized in Table 1 and Figure 1. Two thirds of the group are women; 85% (175) were hospitalized at onset; and almost all (95%) of the respondents sustained paralysis of one or more limbs, indicating that this group, in general, experienced a fairly severe, acute infection. The median age of the respondents was 49 years, with a range from 28 to 80 years. While the majority of the study group (60%) were between the ages of 40 and 59, there was a sizable group under 40 (17%) and over 59 (22%). The distribution of the year of onset of polio ranged from 1909 to 1963, with half of the respondents acquiring polio in 1949 or later, the peak year being 1952. The number of years the respondents have had polio reflects the same distribution from a different perspective with a median duration of 34 years and one quarter, or 53, having had the disease for 40 years or more. Since onset of polio, 63% have been married and 95% have been employed full- or part-time.

Figure 1 shows the age at onset for each decade beginning

Table 1. Selected Characteristics of Respondents

	Sex			*Hospitalized at Onset*			*Paralysis at Onset*	
	N	*%*		*N*	*%*		*N*	*%*
Men	64	32	yes	175	85	yes	192	95
Women	137	68	no	26	15	no	9	5
TOTALS	201	100		201	100		201	100

	Current Age			*Duration of Polio*	
	N	*%*		*N*	*%*
<30 yr	4	2	<30 yr	33	16
30-39	30	15	30-39	115	57
40-49	64	32	40-49	27	13
50-59	56	28	50-59	13	7
60-69	36	18	60-69	9	5
>69 yr	8	4	>69 yr	4	2
TOTALS	198	99		201	100
Median	49 yr			34 yr	
Mean	50 yr			37.4 yr	
Mode	47 yr (13)			31 yr (27)	
Range	28-80 yr			20-74 yr	

in 1910. Although the numbers are relatively small for the early decades, there is a steady increase in the age of onset over the years. In the 1920s and 1930s, 10% and 36%, respectively, were 10 years of age or older at onset of polio, while in the 1940s and 1950s, these percentages increased sharply to 56% and 71%, respectively. The median age of the respondents who acquired polio before 1949 was 8 years compared to a median age of 16 years for those affected in 1949 or later. There was also an in-

Comparison of Age at Onset Distribution of Poliomyelitis Cases (Paralytic and Non-Paralytic) for Massachusetts 1912-1952 (A) with Respondents to Questionnaire 1910-1959 (B)

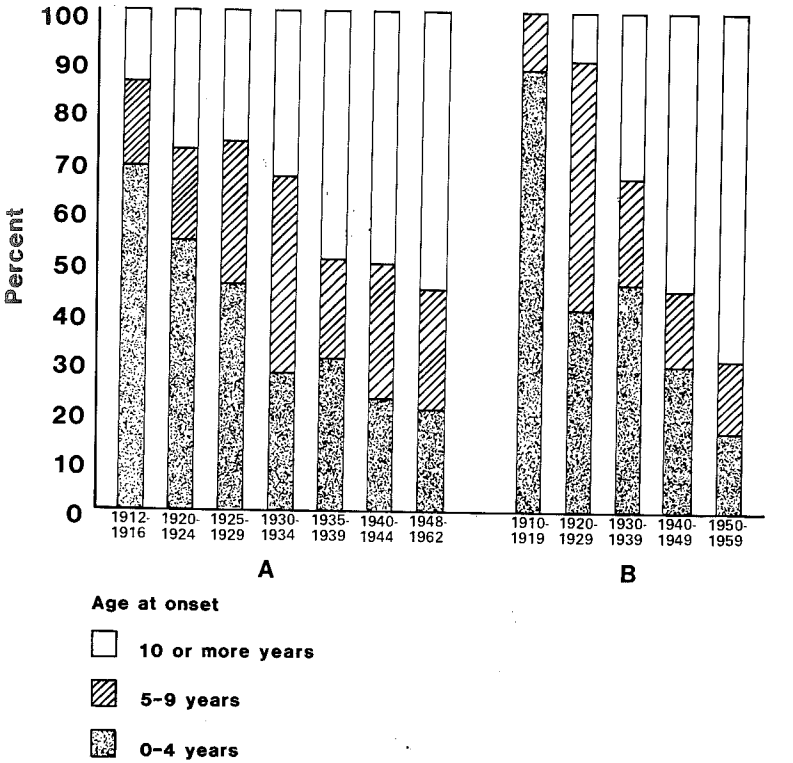

FIGURE 1

crease in ventilator use at onset over the decades, which reflected an increase in severity of illness as paralytic polio afflicted older age groups. Table 2 summarizes ventilator use by age of onset. Slightly over 16% of respondents who acquired polio under the age of 10 required a ventilator compared with 35.7% who were 10 years of age or older at onset and used a ventilator. The median age at onset of persons who required a ventilator was 17 years compared with a median age of 9 years for those who did not use a ventilator. The increasing age at onset and increased severity of polio in the older age groups seen in this population were the same trends that characterized polio in this country during the first six decades of this century.[8]

Changes from Onset of Polio to Present

Regardless of the initial severity, most respondents experienced some measure of neurological and functional recovery which eventually reached a maximum level a median of 6 years post-onset. This period of maximum recovery was variable, but in the study group lasted a median of 26 years and then was followed by a period of decline in a large number of persons who experienced significant new health problems and functional changes. Table 3 summarizes these changes for three intervals: onset, the period of maximum recovery and the present with respect to the use of ventilators, wheelchairs, ambulatory aids (e.g., braces, crutches) and personal assistance in performing daily activities.

The most dramatic changes occurred for wheelchair and ventilator use: 131 (65%) of the respondents required a wheelchair

Table 2. Number of Respondents by Age at Onset of Polio and Ventilator Use at Onset

	Ventilator Use		
Age at Onset	*No*	*Yes*	*Percent Yes*
0-4	48	6	11.1%
5-9	24	8	25.0%
10-14	30	7	18.9%
15-19	15	14	48.3%
20-24	13	8	38.1%
≥25	14	11	44.0%
	144	54	

during the initial illness. Wheelchair use then dropped to 78 (40%) by the time maximum recovery was achieved. Since maximum recovery, however, the number requiring a wheelchair has increased sharply by 50% to 117 (59%) of the group. Patterns of ventilator use showed even larger changes. Fifty-four respondents needed partial or total ventilatory assistance at onset compared with only ten during the period of maximum recovery. The number of persons requiring a ventilator now is 18, or 9% of the group—an increase of 80%. Less dramatic, but similar changes were found for persons requiring ambulatory aids and personal assistance to perform daily activities.

New Health and ADL Problems

In addition to the relatively objective changes of wheelchair and ventilator use, there were a number of relatively subjective changes reported by the respondents. These were grouped into two categories: new health problems and new problems in activities of daily living (ADL). Table 4 ranks the areas that demonstrated the most change for all respondents. Among the new health problems, fatigue was reported most commonly (87.3%), followed by weakness in previously affected muscles

Table 3. Number of Respondents by Category of Involvement

Required Partial or Total	*Onset*		*Maximum Recovery*		*Now*	
	N	%	*N*	%	*N*	%
Ventilator use						
Yes	54	27	10	5	18	9
No	146	73	189	95	181	91
Wheelchair use						
Yes	131	65	78	40	117	59
No	68	35	119	60	81	41
Ambulatory aids						
Yes	139	70	112	56	119	60
No	61	30	87	44	80	40
Personal assistance						
Yes	177	91	84	43	95	49
No	18	9	112	57	100	51

Table 4. Most Frequent New Health and ADL Problems* Since Achieving Maximum Recovery

	Total (N = 201)
New Health Problems	*Percent With Problems*
1. Fatigue	87.3
2. Weakness in previously affected muscles	81.5
3. Muscle pain	75.5
4. Joint pain	75.4
5. Weakness in previously unaffected muscle	71.3
6. Breathing difficulties	41.9
New ADL† Problems	
1. Walking (N = 156)	82.2
2. Climbing stairs (N = 157)	81.4
3. Bathing	61.1
4. Transfers	51.2

*ADL = activities of daily living.
†Numbers in parentheses are respondents at risk for that problem.

(81.5%), muscle pain (75.5%), joint pain (75.4%), weakness in previously unaffected muscles (71.3%), and new difficulties with breathing (41.9%). Other new health problems were reported much less commonly. Since achieving a period of maximum recovery, 37.4% reported a need for more sleep, 21.8% experienced problems with headaches, 19.2% experienced difficulties with their voice, 17.9% have had personality changes, 12.7% reported sensory changes, and 9.0% reported difficulty with nightmares.

Fatigue was usually described as overwhelming exhaustion accompanied by a marked change in level of energy and endurance. It was commonly brought on by activities that had been carried out on a daily basis for years without special effort or noticeable sequelae. Of all the new health problems, this seemed to be the most distressing since it imposed new limits on people's lives without obvious objective changes that others could easily identify. Many respondents found they could reduce the fatigue by decreasing or altering their daily routines.

Muscle pain was often described as deep and aching and for many respondents was similar to the muscle pain experienced during their acute illness years earlier. Rest or decreased level of activity frequently improved the pain, as did salicylates, dry heat or hot baths. Joint pain was most commonly associated with activity and improved with rest, nonsteroidal anti-inflammatory medications and a change of routine. Muscle weakness was particularly noticeable in endurance-type activities and seemed to respond best to curtailment of activities. A number of respondents were put on vigorous exercise regimens by their physicians that markedly aggravated their weakness, some permanently.

Among the ADL problems, new difficulties with walking were reported most frequently (82.2%), followed by difficulty in climbing stairs (81.4%), with bathing (61.1%) and with transfers (51.2%). Other ADL areas that have been associated with new difficulties occurred somewhat less frequently. Since reaching maximum recovery, 48.9% said they have experienced new difficulties with bladder function; 45.2%, with dressing; 31.8%, with sexual function; 22.0%, with eating or swallowing; 15.1%, with bowel function.

Changes at 40 Years Post-Polio for Hospital and Nonhospital Groups

In addition to investigating new problems and their frequency in the total group regardless of the duration of polio, we analyzed only those who had had polio for at least 40 years to equalize the time at risk for each person to develop one or more difficulties. Further, because many of the symptoms reported in this study were fairly nonspecific and their frequency in an age- and sex-matched sample of the general population was unknown, we developed a preliminary estimate of magnitude of changes occurring in some polio survivors by comparing the experience of those hospitalized at onset with the group not hospitalized. While the nonhospitalized respondents were not an ideal control group, they provided a readily available population who had experienced a mild form of the same or similar illness many years ago. Respondents hospitalized at onset are compared with those not hospitalized in Table 5. These groups were fairly similar when compared for sex and current age; however, those factors

Table 5. Comparison of Key Variables for All Respondents and Those Hospitalized and Nonhospitalized at Onset of Polio

	All Respondents (N=201)	*Hospitalized (N=176)*	*Nonhospitalized (N=25)*
Current age (median)	49 years	49 years	53 years
Sex			
Men	64 (32%)	58 (33%)	6 (24%)
Women	137 (68%)	118 (67%)	19 (76%)
Age at onset (median)	10 years	12 years	3 years
Extremities paralyzed* at onset			
All 4 limbs	112 (56%)	107 (61%)	5 (20%)
Only 1 limb	11 (5%)	7 (4%)	4 (16%)
Ventilator at onset			
Yes	54 (27%)	54 (31%)	0 (0%)
No	146 (73%)	120 (69%)	25 (100%)

*Paralysis or paresis.

associated with increased severity such as age at onset, number of limbs paralyzed and ventilator use were markedly different. The median age at onset for the hospitalized group was 12 years compared with 3 years for the nonhospitalized group. Of the hospitalized group, 61% experienced paralysis or paresis of all four limbs compared to 20% in the nonhospitalized group; 31% of those hospitalized required a ventilator at onset compared to none in the nonhospitalized group. Using life table techniques with censored data, we examined respondents with polio 40 years by hospital status at onset for new health and ADL problems. Table 6 summarizes in rank order the results of these analyses for those hospitalized and not hospitalized at onset of polio, listing the percent who experienced each problem by 40 years, and for the population at risk, the median time and standard error from polio to the onset of each problem. The level of significance between the experience of the hospitalized and nonhospitalized groups was determined using the generalized Savage (Mantel-Cox) test of significance. For nine of the ten new health and ADL problems studied, there was a significant difference between the two groups. The problem of fatigue was reported most frequently by 73% of the hospitalized group compared with 25.7% of the nonhospitalized group, which was significant at the 0.00001 level.

Table 6. Percent of Polio With New Health and ADL Problems* 40 Years After Onset of Polio and Median Time to Onset of Problems for those Hospitalized and Nonhospitalized at Onset

	Hospitalized (N=176)		*Nonhospitalized (N=25)*		
New Health Problems	*Percent With Problems at 40 yr*	*Median Time† (yr) ± SE to Onset of Problems*	*Percent With Problems at 40 yr*	*Median Time† (yr) ± SE to Onset of Problems*	*p*
1. Fatigue	73.0	29.8 ± 1.0	25.7	—	<0.00001
2. Muscle pain	63.5	33.9 ± 1.5	20.3	—	<0.0009
3. Joint pain	61.6	35.0 ± 2.2	24.9	52.4 ± 6.7	<0.0042
4. Weakness in previously affected muscles	63.0	34.4 ± 2.2	17.8	55.8 ± 10.8	<0.0001
5. Weakness in previously unaffected muscles	46.1	42.6 ± 4.4	21.7	59.3 ± 4.7	<0.0077
6. Breathing difficulties	34.8	—	9.4	—	<0.0112
New ADL Problems‡					
1. Walking	58.8 (N=133)	34.4 ± 3.9	31.2 (N=25)	—	<0.0085
2. Climbing stairs	55.9 (N=134)	36.9 ± 2.6	26.8 (N=25)	—	<0.0070
3. Bathing	28.8 (N=176)	—	4.1 (N=25)	—	<0.0009
4. Transfers	29.0 (N=76)	—	0 (N=2)	—	<0.1485

*ADL = activities of daily living; †median time and standard error from onset of polio to occurrence of each problem; ‡numbers in parentheses are respondents at risk for that problem.

The median time from polio to onset of fatigue for the hospitalized group was 29.8 years, while the median time for the nonhospitalized respondents was not achieved by the time of this study.

The difference in percentages of those who experienced other new problems at least 40 years post-polio ranged from a 1.9-fold increase for new difficulty with walking to a 7-fold increase for

new problems with bathing in the hospitalized group compared to the nonhospitalized group. Where comparison data were available, the difference between the two groups for the median number of years post-polio to the onset of new problems was considerable. This difference ranged from 16.7 years for weakness in previously unaffected muscles (42.6 years for the hospital group compared with 59.3 years for the nonhospital group) to 21.4 years for weakness in previously affected muscles (34.4 years for the hospital group compared with 55.8 years for the nonhospital group). The number of persons analyzed for new ADL problems varied for each activity, based on the number at risk for developing that problem. For example, all those who used a wheelchair full-time during the period of maximum recovery were excluded from consideration for new problems with walking.

Variables Associated With Developing New Health Problems

Although many new health and ADL problems were very common in the study group, not all respondents were at equal risk for developing them. Since the duration of polio ranged from 20 to 74 years, there was a large variation in the number of years respondents were at risk for developing new problems. To compensate for varying lengths of time since onset, we restricted our statistical analysis to subgroups who had polio an equal number of years. The 40-year cohort analysis was the most useful because it provided the median time to onset for the most problems. However, whether we used this cohort (which included 26% of respondents) or the 30-year cohort (which included 84%), the variables at onset which showed a consistently strong association with developing the late effects of polio many years later remained the same, namely: required hospitalization, were over 10 years of age, required a ventilator and experienced paralysis or paresis of all four limbs. Sex was not significantly associated with developing any of the new problems studied, although the trends suggested women were more at risk than men. Table 7 summarizes these four variables and gender with respect to the problem of fatigue and lists the percent in each variable grouping who developed the problem, the median time from polio to onset of the problem and the level of significance between the variable groups using the generalized Savage (Mantel-Cox) test.

Similar differences were found for other new health and ADL problems as well.

New Health and ADL Problems by Current Age

To estimate the effect of aging on the occurrence of new health and ADL problems, we looked at the percent of respondents who reported new difficulties in three age groups: 40 years old and under, 41 to 59 years of age, and 60 years old and over. Table 8 summarizes the results of three new health and ADL problems which represented the most common patterns found. In most instances, the 41- to 59-year-old group reported the highest percent of problems (e.g., fatigue and climbing stairs). Less commonly, the 40-year-old and under group had the highest percent of problems (e.g., weakness in previously affected muscles). By contrast, the 60-year-old and over group did not have the highest percent of problems for any of the ten new health and ADL areas studied.

Table 7. Variables Associated With Polio Survivors Developing New Health Problem of Fatigue at 40 Years

Rank Order	*Variables*	*N*	*Percent With Problem*	*Median Time (yr)* ± SE to Onset of Problem*	*p*
1.	Hospitalized at onset				
	Yes	176	73.0	29.8 ± 1.0 yrs.	<0.00001
	No	25	25.6	55.7 ± 6.1 yrs.	
2.	Age at onset				
	≤ 10 yr	93	53.4	37.8 ± 3.9	<0.00001
	> 10 yr	104	83.0	29.3 ± 1.6	
3.	Ventilator at onset				
	Yes	54	75.9	27.6 ± 1.2 yrs.	<0.0029
	No	146	54.8	34.0 ± 2.1 yrs.	
4.	Extremities paralyzed† at onset				
	All 4 limbs	105	73.2	29.2 ± 1.1 yrs.	<0.0240
	Only 1 limb	11	57.7	35.6 ± 1.4 yrs.	
5.	Sex				
	Male	64	52.5	36.4 ± 7.9	<0.1894
	Female	137	71.3	31.0 ± 3.0	

*Median time and standard error from onset of polio to occurrence of problem.
†Paralysis or paresis.

Table 8. Percent of Respondents for Three New Health and ADL Problems by Current Age

New Health or ADL Problems	*≤40 Years (N=44)*	*41 to 59 Years (N=110)*	*≥60 Years (N=44)*
Fatigue	79.2	85.2	75.2
Weakness in previously affected muscles	83.4	79.5	73.1
Climbing stairs*	53.4 (N=34)	90.8 (N=86)	64.0 (N=36)

*Numbers in parentheses are respondents at risk for that problem.

Non-Polio Chronic Diseases

In addition to reporting new health and ADL problems, respondents indicated any other chronic diseases they had experienced since the onset of polio. Using life table techniques with censored data, we examined all persons with polio 40 years or more by their hospital experience at onset. Table 9 summarizes the results of these analyses for the five most common chronic diseases, listing the percent diagnosed with each disease by 40 years and for each group, the median time and standard error from polio to the diagnosis of each disease. The level of significance between the experience of the hospitalized and

Table 9. Percent with Chronic Diseases and Median Time to Onset 40 Years After Polio for Hospitalized and Nonhospitalized Groups

	Hospitalized (N=176)		*Nonhospitalized (N=25)*		
Chronic Disease	*Percent with Disease at 40 yr*	*Median Time* (yr) ± SE Onset of Disease*	*Percent with Disease at 40 yr*	*Median Time* (yr) ± SE to Onset of Disease*	*p*
1. Hypertension	33.3	57.9 ± 12.8	4.5	—	<0.0029
2. Respiratory disease	29.6	—	11.8	—	<0.1581
3. Arthritis	26.4	58.8 ± 24.2	4.0	67.1 ± 8.9	<0.0403
4. Heart disease	23.8	—	4.7	—	<0.0809
5. Neurological diseases	7.5	—	4.7	—	<0.8702

*Median time and standard error from onset of polio to occurrence of each chronic disease.

nonhospitalized groups was determined using the generalized Savage (Mantel-Cox) test of significance. For two of the five chronic diseases examined, there was a significant difference between the two groups. Hypertension was reported most frequently in the hospitalized group (33.3%) followed by respiratory disease (29.6%), arthritis (26.4%), heart disease (23.8%) and non-polio neurological diseases (7.5%). The frequency of these diseases in the nonhospitalized group was substantially less, ranging from 4% for arthritis to 11.8% for respiratory disease. Median time from polio to the diagnosis of these diseases for the hospitalized group was approximately 58 years or more than 20 years later than the onset of most of the new health and ADL problems experienced by the same group.

The Fatigue Phenomenon or the Polio Wall

In a subgroup of 50 respondents, we asked if they had ever experienced, since achieving maximum recovery, the rather sudden onset of one or more symptoms together, such as intense fatigue, headache, weakness, hot and cold flashes, sweating or a feeling like hitting a "wall." Of those queried, 25 (50%) reported experiencing this phenomenon. Of the 25, 80% were full-time ambulators, 16 were women, the median age was 43.5 years and the median age of onset of polio was 14 years. Also, 18 (70%) required a ventilator at onset; 17 (68%) had quadriplegia; and 23 (92%) were hospitalized at onset. The median time to onset of these symptoms from the onset of polio was 34 years, and 17 (68%) said they occurred on a daily basis. Most commonly, the polio "wall" was experienced in mid- to late afternoon—although some reported it in the morning—and could be aborted or ameliorated by increasing rest time, napping or reducing the overall level of activity during the day.

Respondents' Comments

Following each closed-ended question, respondents were invited to add other information or comments concerning their history. One hundred forty-five (73%) appended comments that ranged from a few sentences to several single-spaced, typewritten pages. In general, the comments can be grouped into three categories: anger, frustration and relief. The anger concerned the

fact, as some put it, that they felt they were getting polio all over again. Many described their muscle pain, for example, as being similar to the pain they had experienced during the acute episode. Others described their long battle to achieve functional and economic independence, only to discover as they entered the middle years of their life that a new battle was beginning against an unknown process with an unknown outcome. The frustration was directed at the medical profession that usually had no or little information regarding the late effects of polio and could provide no specific treatment or management principles. Because of the dearth of information in the medical literature, most physicians are understandably unaware of the possibility of the late progression of polio, whether in the form of PMA or some other phenomenon. As a result, many respondents commented they could not get their physicians to believe they were having difficulties or to validate their fears and their new struggle. This was especially frustrating for respondents who experienced rather dramatic changes, but did not demonstrate major new findings on physical examination. Frequently, their complaints were dismissed as a form of malingering or neurotic behavior. The relief was expressed in response to learning that something was now being done (even if only asking questions) and discovering that others were experiencing similar changes.

Discussion

The data presented here describe the late effects of polio in a group of 201 questionnaire respondents. Although there are major methodological limitations to this kind of study, some general patterns emerged which suggest that many of these polio survivors may be experiencing a common phenomenon. Whether this phenomenon constitutes a true post-polio syndrome or a cluster of unrelated clinical events it is not possible to say from these data. However, based on the results of this study, five distinct features of this phenomenon were apparent: (1) the natural history of chronic polio presented a characteristic and fairly common pattern; (2) there was a definite and sometimes dramatic decline in health status which began to occur between 30 and 40 years following the acute attack of poliomyelitis; (3) there were a number of factors present at onset of the disease which were strongly associated with developing new problems

many years later; (4) the changes in health and ADL status occurred with approximately the same frequency in young and old persons and (5) other chronic diseases occurred less frequently and more than 20 years after the late effects described earlier.

The natural history of chronic polio among these respondents included four phases: (1) antecedent occurrence of severe poliomyelitis in childhood or later in life; (2) partial to fairly complete neurological and functional recovery; (3) a period of stabilization of maximum recovery lasting many years, usually 20 or more; and (4) a gradual or sudden onset of one or more changes in health status and functional ability. Sometimes these changes were preceded by a minor accident, fall or period of bed rest, and sometimes they occurred without any apparent provoking incident.

The decline in health status began most commonly with the onset of fatigue which was reported by 87.3% of respondents and occurred a median of 32.5 years post-polio. The other most common problems were muscle pain, joint pain and weakness in previously affected and unaffected muscles which occurred at a median time of 35.7 to 46.2 years following polio. A measure of the extent of the weakness experienced by the study group was the finding that 39 persons, or almost 20% of respondents, have had to return to partial or full-time use of a wheelchair after many years of being wheelchair-free. These new health problems were frequently accompanied by new changes in ADL. Over 80% reported new difficulty with walking and climbing stairs, which occurred at a median time of 38 years following polio, and approximately 50% to 60% reported new difficulties with bathing, transfers and bladder function.

Four factors present at onset were stongly associated with developing the late effects of polio many years later. These were (1) hospitalization at onset; (2) contracting polio over the age of 10; (3) ventilator use; and (4) paralysis in four limbs at onset. For persons who had any one of these four risk factors, the median time post-polio to onset of fatigue was *under 30 years.* Of these four risk factors, the need for hospitalization, ventilator use and paralysis in four limbs, in all likelihood, reflected a common underlying variable—namely, severity at onset. Thus, the two most important predictors of whether someone would develop late changes and when were age at onset and severity at onset. Although women had more problems and developed them earlier

than men, sex was not significantly associated with developing any of the new health or ADL problems studied. A composite of the typical respondent in this study with the late effects of polio was a 48-year-old woman who contracted severe paralytic polio requiring a ventilator in 1950 at the age of 15 and began having new health problems—especially fatigue, weakness and muscle pains—in 1980 or 30 years post-onset.

The role of aging in causing the late effects of polio is unclear at present. The conventional wisdom in the past has been that progressive weakness in older polio survivors was simply a function of an accelerated aging process attributed to the loss of anterior horn cells of reinnervated motor units. Since these cells controlled a greater percentage of the muscle function than normal neurons, their loss resulted in greater clinical weakness than is seen in the normal aging of a non-polio person. If motor neuron loss with advancing age were a determining factor, then one would expect to find a steady increase in new difficulties as the population at risk became progressively older. In fact, the respondents in this study showed approximately the same frequency of new problems across all age groups. Although we were unable to isolate the aging variable entirely in our analyses, the results suggest that some process was set in motion at the time of the acute infection, which then manifested itself at a more or less fixed interval many years later.

The question of why this phenomenon appears to be making itself known only recently is an intriguing one. Part of the explanation may lie in the fact that we are seeing for the first time the combined effects of large epidemics in the late 1940s and 1950s which affected people at an older age group and with more severity. These people are now 30 to 40 years post-onset, are from 45 to 60 years old and reaching a critical point in the aging process. Thus, the effects of polio and aging may be "catching up" with them simultaneously. Possibly, the phenomenon described here represents a variant of aging and because of prior illness uncovers a process which permits accelerated aging to occur. In this sense, the late effects of polio may provide a model in which to study the aging process. Any explanation of this problem, however, must take into account the fact that a sizable number of young persons are encountering difficulties. Of the 44 persons 40 years or younger in this study, 38 (86.4%) reported experiencing one or more problems.

In contrast to the cluster of new health and ADL problems described by the respondents in this study, the occurrence of other chronic conditions presented a very different pattern. Among those hospitalized at onset, the median time to the diagnosis of hypertension and arthritis was approximately 58 years or more than 20 years after the onset of most of the new health and ADL problems experienced by the same group. Furthermore, the variation in time from polio to diagnosis, as reflected by the standard error, was extremely large compared to the relatively small standard errors found with most of the new health and ADL problems.

How representative these data are of the larger population of people who contracted polio and are still living is also unknown. Undoubtedly, the percent of people having difficulty is considerably lower than that reported here because of the tendency of people with problems to respond to a questionnaire. In addition, many of the symptoms reported in this study were fairly nonspecific, and it is unknown how frequently these problems occur in a representative sample of the general population matched for age and sex. Using the nonhospitalized respondents as a preliminary control group for purposes of comparison, we found that the hospitalized group experienced more than three times as many problems up to 21.4 years earlier in nine out of ten areas studied.

Why there were more women than men in our sample is not clear. In the general population, it is likely there are at least as many if not more men than women with polio still alive, since in children up to age 15, polio was considerably more common in males, while it was more common in females among adults aged 15 to 39.[8] In the study group, there was no statistically significant sex bias for any of the problems investigated, although the trends suggested that women were experiencing more problems than men, which supports an earlier study that showed women developed more severe polio than men independent of age.[9]

With the exception of sex, the epidemiological characteristics of the respondents resembled the epidemiological patterns of polio, in general, during this century. From earlier studies, it is well known that polio afflicted mostly young children at the turn of the century and then became increasingly a disease of older children, adolescents and adults.[8-12] Figure 1 shows a com-

parison of the age at onset using data from Massachusetts from 1910 to 1954 with the age at onset of our respondents. The major differences are found in the 1910s and 1920s and can be accounted for by the small number of respondents acquiring polio in those decades in our study group.

Concomitant with a rise in age at onset over the years, the disease also showed an increase in severity among older age groups. Weinstein et al in 1952 reported on 259 hospitalized patients with spinal paralysis from polio and found that monoplegia occurred most commonly under 16 years of age, while quadriplegia occurred 2.5 to 3 times more frequently in adults than in those under 16 years.[9] In our study, the same trends were apparent. Ventilator users were 2.6 times more common in those 15 years of age or older at onset than in those under 15, and quadriplegia was 1.6 times more frequent in the older group.

Although there is no known cure for the late effects of polio reported here, proper management begins with excluding treatable conditions, in particular, obesity, tendonitis, myofascitis and neuromuscular problems. Reducing the level and intensity of activity to stay within limits of comfort was helpful to a number of respondents. Increased rest during the day was beneficial for some, while others found it necessary to make major alterations in their life style and even change their jobs to minimize the new health problems. Still others discovered the best way of coping was to resume use of a brace, wheelchair or ventilator, either full-time or part-time, or increase their reliance on someone else to assist with certain daily activities. At the same time, some people reported an aggravation of their symptoms, especially an increased loss of strength or function, apparently as a result of intense exercise programs or endurance activities designed to rebuild tired muscles or increase their strength and endurance. Based on these comments and our own clinical experience, we believe that until more specific therapy is available, persons with a history of polio—with or without neurological progression—should undertake an exercise program and strenuous activities with caution. Remaining as active as possible within the limits of comfort and interrupting extended activities with periodic rest periods is prudent advice at this stage of our knowledge.

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Differential Diagnosis of Pain and Weakness in Post-Polio Patients

Frederick M. Maynard, M.D.

Introduction

Increasing weakness and pain are frequent problems for patients with residual neuromuscular dysfunction from previous polio. In a recent questionnaire survey of 403 post-polio patients distributed by the Roosevelt Warm Springs Institute for Rehabilitation, 70% of patients reported pain and 84% reported a recent change in muscle strength or endurance (Ann Bailey; unpublished data, May 1983). There are many potential etiologies for these problems, considering the wide variety of residual muscle imbalances, orthopedic deformities and compensatory functional adaptations seen in these patients. One possible etiology is the so-called post-polio syndrome of progressive muscular weakness from further amyotrophy of muscles previously involved by polio. Amyotrophy is understood to mean a loss of functioning anterior horn cells, resulting in muscle atrophy and weakness. Slowly progressive amyotrophy resulting in a gradual decrease in maximum strength and/or endurance of muscles previously involved by polio puts overuse strain on functionally useful muscles, tendons, ligaments and joints, which can be expected to produce a wide variety of musculoskeletal pain and motion problems. Increasing weakness can also create a variety of problems in carrying out daily activities of mobility, self-care, vocation and recreation.

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Evaluation Approach

In order to explore the post-polio syndrome, a post-polio clinic was established by the Department of Physical Medicine and Rehabilitation at the University of Michigan Medical Center. The clinical approach to evaluation of these patients had three major components:

1. A careful history was taken to determine specific changes in neuromuscular function and strength in relationship to the patients' lifestyle adaptations to any residual neuromuscular impairments or orthopedic deformities from previous polio. The specific relationship of exercise, exertion and repetitive use of muscles to complaints of pain, weakness or fatigue was established by careful review of activity patterns.

2. A careful, biomechanical evaluation of the presenting problems was made in view of current muscle strength, joint range of motion and joint deformities.

3. Electrodiagnostic studies were carried out whenever indicated and permitted.

Criteria for a diagnosis of post-polio syndrome were (1) a history of decline in maximal strength of muscles previously involved by polio that is not explained by another diagnosis and/or a clear history of transient muscle fatigue, weakness, or myalgia following exercise or prolonged use of involved muscles and (2) electrodiagnostic evidence of motor unit changes consistent with previous polio involvement in symptomatic muscles.

Results of Evaluation

During a two-year period, 30 patients (25 women and 5 men) were evaluated at the post-polio clinic. Eighteen patients met the above criteria for a diagnosis of post-polio syndrome. The average age at the time of clinical evaluation for patients diagnosed as having post-polio syndrome was 50 years (range: 34-65). The average age of having had acute poliomyelitis was 13 years (range: 2-31). The average interval from acute polio to onset of post-polio syndrome symptoms was 31 years (range: 20-53). Patients were seen in the clinic on an average of six years after onset of post-polio syndrome symptoms. Among the 12 post-polio patients evaluated who were not diagnosed as having post-polio syndrome, the average age when seen was 49 years (range: 31-80) and the

average age of acute polio was 7.8 years (range: 1-16). Fifteen of the 18 patients (83%) with post-polio syndrome had been ambulatory following recovery from acute polio. Seven of the 12 patients (58%) not having post-polio syndrome were ambulatory. This difference between the two groups suggests that ambulatory patients may more frequently develop progressive amyotrophy, perhaps from chronic overuse of weakened muscles. Ambulatory patients may also be more aware of modest decreases in strength and more readily seek evaluation. The onset of post-polio syndrome symptoms was slow in 15 of the 18 patients. Three patients reported a sudden onset of symptoms (days to weeks) affecting one patient after trauma.

Chief Complaints

The chief complaints among the 18 patients diagnosed as having post-polio syndrome were decreasing strength (9), pain (8), and greater trouble breathing (1). Post-exercise fatigue and transient decrease in strength were prominent symptoms in eight patients. Post-exercise myalgia was a prominent symptom in five patients. Four patients reported the onset of symptoms following several months of participation in aerobic or other conditioning exercise programs. Fasciculations were a prominent symptom or observed finding in only three patients, including one patient who was not diagnosed as having the post-polio syndrome.

The chief complaints among the 12 patients not diagnosed as having the post-polio syndrome included musculoskeletal pain (6), equipment problems (3), breathing problems (1) and progressive orthopedic deformity (1). One patient presented with the complaint of post-exercise myalgia and more trouble walking, but was excluded from the post-polio syndrome diagnostic group because of a normal EMG in the symptomatic muscles. Two of the patients with pain complaints were diagnosed as having symptomatic carpal tunnel syndrome. One patient who presented with complaints of increasing difficulty breathing had a long history of restrictive lung disease as a residual from polio, but did not have any measurable changes in pulmonary function. He died suddenly several months after being seen, apparently from respiratory failure.

Musculoskeletal Pain

Musculoskeletal pain problems consisted of back pain in five patients, neck pain in six patients, and shoulder pain in nine. Six of the nine patients with shoulder girdle muscle complaints had a correlation between their symptoms and their use of canes or crutches for ambulation. None of the shoulder pain patients had x-ray evidence of degenerative arthritis in the glenohumeral or acromioclavicular joints. Shoulder girdle pain complaints were attributed to nonspecific overuse strain (2), shoulder bursitis (2), tendonitis and myofascitis (3), epicondylitis (1) and chronic glenohumeral subluxation (1). Back pain was attributed to chronic muscular strain in four cases, one associated with scoliosis and one with pelvic asymmetry from leg length discrepancy. Back pain in one patient followed a fall resulting in a hematoma of upper thoracic paraspinal muscles. Neck pain was attributed to cervical muscle strain and chronic tension (2), atlantoaxial osteoarthritis (1) and cervical spondylosis (3). Based on clinical examination and response to cervical traction, a diagnosis of cervical disk degeneration without radiculopathy was considered possible in two of the three cases with cervical spondylosis.

Six of 18 patients who underwent electrodiagnostic examination had slowed conduction of the median nerve at the wrist. However, only two had significant symptoms related to carpal tunnel syndrome. Four of these six patients walked using upper extremity ambulation aids. The two symptomatic patients had some response to modification of the crutch handle. Three patients had degenerative arthritis of the thumb or index finger joints and all were ambulatory using upper extremity aids.

Nineteen of the 30 patients were told to alter their activity to decrease strain and/or excessive exertion of involved muscles. Nine patients were specifically advised to do this to minimize potentially harmful amyotrophy from overuse. In ten patients, a change of activity level was advised for management of musculoskeletal pain problems. Alterations in mobility that were advised included the new use of a cane or crutch (3), new use of a brace (3), discontinuation of any limited ambulation (2), new use of a wheelchair (1) or new use of an electric wheelchair (6). This experience of increased need for mobility aids is similar to that reported by Anderson et al.[1]

Electrodiagnostic Testing

Electrodiagnostic evaluations were carried out in 15 of the 18 patients who were diagnosed as having post-polio syndrome. All 15 patients showed motor unit changes consistent with a chronic neuropathic process, which included increased amplitude and duration of motor unit action potentials, increase in percentage of polyphasic motor units and decrease in number of motor units on maximum recruitment. Four patients showed some spontaneous activity (positive waves or fibrillations) in some of the symptomatic muscles. Two patients had prominent fasciculations. A single fiber study of one patient showed a normal jitter and an increase in fiber density, suggesting chronic but not acute denervation. One patient had had a muscle biopsy performed at the Mayo Clinic, which was interpreted as showing nonspecific changes of neurogenic atrophy. Repetitive stimulation studies done on three patients were normal. These findings are similar to those reported by Hayward and Seaton,[2] who studied 24 asymptomatic old polio patients. They also found motor unit changes of chronic denervation in all muscles previously involved by polio and only a few patients with fasciculations or spontaneous activity.

Review of this clinical experience suggested that post-polio syndrome frequently causes problems for patients by provoking musculoskeletal pain syndromes, as well as by decreasing strength, which alters functional abilities. Treatment of musculoskeletal pain syndromes is complicated by further disuse atrophy associated with resting a muscle to allow healing of inflammation in the contractile musculotendonous units. Efforts to improve strength by gradual and controlled strengthening programs often aggravate the pain problems. The clinical experience with these patients has indicated a poor response to attempts at strengthening involved muscles or improving their endurance through an exercise program. Strengthening exercises often appeared to make their problems worse. Therefore, my approach has been to recommend maintaining strength by continuing important functional activities, such as independent self-care, ambulation, work or recreational activities whenever possible.

Two brief case reports are presented to illustrate the clinical problems seen in post-polio patients.

Case 1

A 64-year-old retired professor of economics reported a history of acute poliomyelitis in 1950 at age 31. He had residual lower extremity weakness, particularly of the quadricep muscles, worse on the left side. Following rehabilitation efforts, he became ambulatory without upper extremity aids by 1952. About 25 to 30 years later, in the middle 1970s, he began using a cane on the right side because of increasing weakness in his legs when walking long distances. In August 1980 he was first evaluated for increasing leg weakness, particularly in his right knee extensors. Examination showed quadriceps strength 4-/5 on the right and 4/5 on the left. Maximal isometric torque produced by the quadriceps with the knee at 90° of flexion, measured on a Cybex apparatus, showed 8.5 ft-lb on the left and 21 ft-lb on the right. Electrodiagnostic examination of the left quadriceps showed 2+ small fibrillations and positive waves, very large amplitude motor unit action potentials that were mostly polyphasic and a very decreased maximal interference pattern. Similar, but less abnormal, motor unit changes were present in the left gluteus medius and anterior tibialis. The patient was advised to perform gentle quadriceps strengthening exercises using 1 ¾ pound ankle weights on the right and 2 ¼ pounds on the left. In December 1980 he fell and fractured his left foot. When next evaluated in August 1981 his strength appeared unchanged. By July 1983, he again noted increasing leg weakness and more difficulty climbing stairs or rising from a chair. Quadriceps strength was graded 2+/5 bilaterally. Strengthening exercises were again recommended using ¼ pound weights. Over the next few months, he increased the weights to one pound, but then discontinued these exercises. When next evaluated in December 1983, he complained of slight further loss of strength and definite post-exercise transient decrease in strength, as after walking a half mile. Knee extensors were 2+/5, with inability to fully extend the knee against gravity. The patient was advised to discontinue quadriceps exercises and avoid exertion to the point of greater weakness. In May 1984 repeat measurements of maximum torque produced by the quadriceps on the Cybex at 90° of knee flexion showed 7 ft-lb on the left and 8 ft-lb on the right. Surface electromyographic recording of the quadriceps during maximum isometric contraction showed no obvious change in size of signal during the 30 to 40 seconds

before fatigue and decline to half of original force. The patient reported no greater weakness than in December 1983.

Case 2

A 37-year-old married housewife had a history of polio at age 5, leaving her with mild residual weakness of the left arm and leg. She underwent surgery on the left ankle at age 9 and was aware of mild shortening of the left leg, but otherwise had no residual problems from polio. She presented at the post-polio clinic in June 1983 complaining of generalized fatigue and weakness. Further history revealed that she had developed a right tennis elbow after taking up tennis five years previously and had surgery for this. A year previously, she began an aerobic exercise class but became very fatigued and "wiped out" after the class. Over the past few months she noted the onset of pain on both sides of her neck spreading into the arms and noted greater fatigue and weakness in her right arm, particularly following prolonged use. Activity history revealed she was a busy homemaker with three children and worked full time at a college for the deaf doing sign language for over 20 hours a week.

Physical examination showed mild scoliosis, a positive left Trendelenburg test and 1 ½" shortening of the left leg. Neck examination was normal. Neurologic examination was remarkable only for 4/5 strength in the right triceps, pronator teres and opponens pollicis. CBC and cervical spine x-rays were normal. EMG showed widespread motor unit changes consistent with previous polio. She was advised to avoid prolonged activities that produced undue fatigue or prolonged pain. She received supportive counseling for depression about her declining strength and reduced activity. Four months later she reported marked increased pain in her shoulders and neck that became much worse after working, doing sign language or housework. Careful manual muscle testing of the shoulders showed 3/5 weakness of the right serratus anterior and 4/5 weakness of all scapular stabilizers, including the trapezius bilaterally. There was a painful arc on shoulder elevation and localized pain on palpation of a thickened supraspinatus tendon. She was advised to discontinue any signing or other strenuous use of her arms. Anti-inflammatory medications and physical therapy treatments with ultrasound and superficial heat were begun. Over the following six months she

required intense activity monitoring, frequent physical therapy and supportive counseling. She terminated her employment. Symptoms continued to fluctuate in intensity in relationship to use of the arms. After three months of almost complete arm activity restriction, except for self-care and light hand activities with arm support, and frequent physical therapy treatments she is asymptomatic and beginning to tolerate very gradual increased exercise and activity with her arms.

Discussion

Although none of the 30 post-polio patients in this group has a history of rapid loss of muscle strength that might suggest a diagnosis of amyotrophic lateral sclerosis or other motor neuron diseases, I have seen such patients. Several reports in the medical literature[3-6] have discussed the relationship between motor neuron diseases and past history of polio. The clinical course of patients described in this report is more compatible with the theory that post-polio amyotrophy is a result of age-related loss of anterior horn cells, which results in symptoms because of already reduced numbers of anterior horn cells. The experience also supports the notion that chronic use of weakened muscles at near maximal loads may speed up these age-related changes. Certainly many of the patients in this series with post-polio syndrome were too young to expect significant age-related loss of anterior horn cells. Most of the muscles with progressive weakness were being regularly used at near maximum loads for daily activities.

Since there are no specific or objective clinical or laboratory findings for the post-polio syndrome yet identified, other diseases of the motor unit must be excluded. A history of rapid loss of muscle strength demands consideration of other possible etiologies for motor neuron disease. A diagnosis of amyotrophic lateral sclerosis can usually be made on the basis of clinical examination for upper motor neuron or bulbar signs and a time course of rapidly progressive symptoms (weeks to months). Electrodiagnostic abnormalities of widespread and prominent spontaneous activity and fasciculations are expected with amyotrophic lateral sclerosis. Nerve conduction studies can rule out generalized peripheral neuropathies and entrapment neuropathies. Electromyographic studies will also confirm the presence of radiculopathy from disk degeneration or other causes.

Radiographic examinations and other studies can rule out any suspicion of carcinoma, which can be associated with amyotrophy. Toxic metal screening tests can be done if there is suspicion of toxin exposure leading to motor neuron disease.

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Anatomy and Pathology

Motoneuron Disease and Recovery in Experimental Poliomyelitis

David Bodian, M.D.

Introduction

During the period of 1944 to 1948, studies were conducted to clarify the relationship between cytopathological changes in the CNS, poliovirus growth and decline, and the clinical course of paralysis and recovery. After the study of spinal cord material from ten fatal human cases, it was decided to determine in infected rhesus monkeys the sequence of cytopathological changes and viral growth that occurs in the spinal cord from the period of onset of preparalytic symptoms to the period of functional recovery in poliomyelitis and to establish the basic features of the cytopathological process in quantitative detail. The changes in the motoneuron population were studied particularly, since motoneuron destruction is the principal cause of motor paralysis and the muscle atrophy that follows. The population unit selected for study was the motoneuron group supplying a single extremity, arm or leg, and consisting of about 14,000 motor nerve cells, at levels C6 to T1, and L4 to L7.

Material

Rhesus monkeys were used to enable study of changes from the earliest period of symptoms to late stages of recovery and to permit more satisfactory fixation and staining of tissues than is possible in human material. In all, 50 rhesus monkeys killed

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from a few days to one year after inoculation with several "strains" of virus of recent human origin were studied quantitatively, and many others were available for qualitative comparisons. These monkeys had been examined in considerable clinical detail, in most cases before they were killed, to determine the time of onset of symptoms, the degree of weakness and the extent of recovery. Motor function of animals was determined by inspection of running, jumping and climbing performance in large cages, by hand examination of individual extremities to determine asymmetry of flexion power and joint extension, and by palpation to detect abnormalities of tone and atrophy. In most cases, daily examinations were made during the acute period of the disease, with weekly and later monthly examinations during the convalescent period. In some animals, voluntary muscle performance was compared with the response to faradic stimulation of nerve points and exposed peripheral nerves at the time of autopsy.

After final clinical examination, animals were anesthetized with ether and perfused through the aorta with 50 ml of normal saline followed by 1 to 2 liters of 10% formol containing 1% acetic acid.

Attention was limited to the changes in the lateral cell columns of the anterior horn of the spinal cord of the brachial and lumbar enlargements, so that histopathological events might be correlated in time and in degree with changes in muscle function of each extremity. Only in this way would it be possible to deal with the dynamics of the disease process. Because of the mixture of stages of cell change found in any one specimen, the precise sequence of events was established by statistical means. As a routine, 50 to 60 sections, out of a total of about 1200 sections in each brachial or lumbar enlargement, were subjected to cell counts. These sections were regularly spaced throughout the cord segments involved, so that 10 to 15 sections were examined as a sample of each of the four principal segments contributing to the brachial and lumbar plexuses, respectively. About 10,000 sections were examined in the study.

Description and Definition of Grades of Paralysis

Limbs were graded as to degree of loss of voluntary muscle power, with flaccidity hereafter termed weakness or paralysis.

Six categories were established arbitrarily, with 5 or "Normal" representing one extreme and 0 representing the other, that of complete flaccid paralysis. Using this grading method excellent agreement was obtained upon independent observations by the same or different examiners. The grading for purposes of this report is defined as follows:

5 - Normal
4 - Definite weakness, but capable of using limb effectively in climbing, running or jumping.
3 - Uses limb poorly in climbing, running or jumping.
2 - Barely able to use limb in climbing or running, but able to move limb segments readily against gravity.
1 - Dangling limb with only feeble movements at skeletal joints.
0 - Complete flaccid paralysis, or only faint traces of movement.

All the gradings were made for maximal possible effort and compared to normal function preceding the onset of paralysis. Since individual animals vary greatly in normal strength depending on size and physical condition, any grading more closely spaced could hardly be comparable from animal to animal or accurate. The above six gradings correspond approximately to those used by Kristensen and Wulff[1] for human cases. In animals in poor physical condition, even these grades cannot be applied with confidence by an experienced examiner, but in healthy, vigorous animals, closer grading could have been used at times. This was especially true in comparing right and left arms or legs, when one member of a pair was slightly weaker than the other. Clinical estimates of muscle power were correlated well with the severity of lesions in anterior horns. In no case was an extremity rated weaker than another in the same animal without a correspondingly greater amount of motoneuron damage in its respective anterior horn. This indicates that a correlation does exist between severity of paralysis and the extent of motoneuron damage.

Basophil Substance

The first microscopic intracellular change seen in motoneurons is the reduction in size and in staining capacity of the basophil bodies.[2,3] This change largely occurs in diffuse

fashion throughout the cytoplasm and is characteristic of most of the abnormal motoneurons seen in the preparalytic period. The frequency of occurrence of different degrees of severity of such diffuse chromatolysis of basophilic substance indicates clearly that this chromatolysis is progressive and may lead in some cases to complete disappearance of basophilic cytoplasmic material within a period of hours or less. In one of the earliest preparalytic cases examined, motoneurons showing mild degrees of diffuse chromatolysis were found in much greater numbers than those showing severe chromatolysis, but this order is reversed in late preparalytic and early paralytic cases. In earlier papers[4,5] the diffuse chromatolysis of early poliomyelitis shows the probable sequence of progression of the process in cells selected from a single preparalytic case. Stages in the continuing progression of degenerative changes, which are probably irreversible, are also described.[4,5]

In the period between three and five days after onset of paralysis, a new morphological pattern of basophilic substance appears. This pattern consists of increased basophilic material adjoining the cell and nuclear membranes, with a central area in the cytoplasm relatively free of the substance. This appearance will be referred to hereafter as "central chromatolysis." After the first week, central chromatolysis is the predominant appearance in injured neurons that are not obviously necrotic, and therefore assumed to be a manifestation of the recovery process. A similar sequence of events occurs in spinal motoneurons regenerating their axons after axotomy.[6]

Our preparations of monkeys with abrupt onset of severe paralysis show clearly that ventral root axons of motoneurons destroyed on the first day of paralysis, and probably many on the preceding day, are morphologically intact until the third day after onset of paralysis, when degenerative changes occur all along the axon length. On the first and second days of paralysis, axons appear to degenerate centrifugally from the cell body for a short distance. It is interesting that even when inflammatory changes are most intense, including neuronophagia, no inflammatory cells of any kind are found anywhere along the axons of cells undergoing active phagocytosis. The conclusion is inescapable from this fact, and from the time course of axonal degeneration, that the primary focus of viral activity is in the

nerve cell body and that when the cell body is destroyed, the axon undergoes typical Wallerian degeneration.

In the subacute stage and later recovery periods, the nuclei of cells with normal cytoplasmic structure are generally normal in appearance as well. Occasionally, however, large persistent acidophilic inclusion bodies are seen in cells of otherwise normal appearance. Since, in the acute stage, such inclusions are seen only in severely chromatolysed cells, their presence later in cells otherwise normal is evidence of the power of recovery of cells damaged by viral action. Such inclusions have been seen in otherwise normal cells as late as 49 days after onset of paralysis. Rarely does one see, in otherwise normal cells, an unusual nuclear "inclusion" consisting of the nucleolus surrounded by a closely packed aggregate of basophilic material. This appearance is also occasionally seen in severely damaged cells.

Pathological Characteristics of Successive Clinical Stages

The Preparalytic Period

The most informative stage in the pathological process is the earliest in which visible changes are apparent. This stage precedes paralysis by about one to three days and gives important information about the sequence of early changes in neurons as well as in the inflammatory response. The important findings may be summarized as follows:

1. The most common visible change in nerve cells in the earliest stage is a diffuse thinning of basophilic substance throughout the cell body, often most conspicuous around the nucleus. Various degrees of this may be seen, but only in the late preparalytic stage is complete dissolution of basophilic substance found in large numbers of cells.

2. Nuclear changes are, as a rule, not apparent until severe cytoplasmic chromatolysis has occurred. The earliest nuclear change is usually the formation of acidophilic nuclear inclusion bodies.

The First Day of Paralysis

In animals in which the onset of paralysis is abrupt, histopathological changes in the spinal cord resemble closely those

seen on the day preceding expected paralysis, but are generally more widespread and more severe. Although the predominant cytopathological stage in motoneurons is diffuse chromatolysis, numerous cells in various stages of necrosis and neuronophagia can usually be seen. Such cells are most common at this time as compared with preceding or following days. Advanced stages of chromatolysis of basophilic material, including complete disappearance of the latter, predominate, with some cells showing cytoplasmic vacuolation or autolysis. Nuclear changes are rarely severe except in cells showing severe chromatolysis.

Second and Third Days

The outstanding feature of the histopathological picture at this period is the scarcity of normal-appearing neurons, even in cases with mild paralysis. Not a single case examined at this period showed more normal cells than 31% of the expected number. This indicates the wide dissemination of virus in the spinal cord of paralytic cases and also supports evidence from other sources, to be considered later, that many cells are invaded by virus and later recover. Residual neurons are predominantly in late stages of diffuse chromatolysis, although, for the first time, cells showing central chromatolysis may make their appearance in appreciable numbers.

At this period, most of the destroyed neurons are completely absorbed, with only focal accumulations of neurophages to mark the spot. Early stages of neuronophagia are also seen, but are not usually as numerous as on the first day of paralysis. In regions of extensive cell loss, even the foci of neuronophagia may have cleared up so rapid is the sequence of changes, and large areas of anterior horn, devoid of nerve cells, may be characterized by a diffuse increase of mononuclear cells.

Four to Six Days

This period is remarkable from the morphological as well as from the functional point of view. Like those in the preceding period, these cases show a very low percentage of normal neurons, even in cases with surprisingly little functional loss and with cessation of paralytic increase. Since very little, if any, active neuronophagia is evident, and since necrotic stages of any sort

are rare, surviving cells would have likely recovered, even though many are severely chromatolytic.

This period is also interesting in showing a reversal of the striking tendency of damaged neurons in the preceding periods to show diffuse chromatolysis in the cytoplasm. Now many cells show aggregation of basophilic substance near the cell and nuclear membranes. Cells showing this type of "central chromatolysis" are mixed with those showing the diffuse type. Occasionally, in the same individuals, one finds cells with diffuse chromatolysis predominating in one spinal cord segment and those with central chromatolysis predominating in a neighboring segment. Eccentricity of nuclear position appears in some cells showing "central" chromatolysis.

Seven to Twelve Days

The principal feature of neuron morphology in this period is the predominance of central chromatolysis in remaining cells other than normal-appearing ones. Cells showing diffuse chromatolysis or necrotic changes, as previously defined, are few in numbers as a rule.

Several features of the pathological picture in this period give evidence that the recovery process is well underway. A greater proportion of normal or almost normal neurons are found than in the preceding period. In some case, numerous cells are seen with normal or almost normal basophil body pattern in which, however, large inclusion bodies are found in the nucleus, indicating previous cytoplasmic changes of a fairly severe degree.

The Third Week

During the third week after onset of paralysis, less than 10% of all neurons are still abnormal in appearance, so rapid is the recovery process. Most of the nerve cells, by this time, are either normal in appearance or destroyed and removed without remaining traces. A few irreversibly damaged cells may be seen in some cases as late as this period, but such persistent "necrotic" cells are negligible in numbers as compared with those quickly destroyed and removed during the first few days of the disease. The predominant pathological state is that of "central" chromatolysis, with evidence of recovery of basophilic substance. Intranuclear inclusions may be present.

Convalescent Stage

The morphological recovery of over 90% of surviving neurons is attained at the end of the first month of the disease. During the next few weeks, as indicated above, the residual chromatolytic cells are negligible in number; moreover, the number of lymphocytes free in the tissues are reduced to very small proportions. It is interesting that the essential disappearance of leucocytic infiltration, which marks the close of the active inflammatory process, should be almost coincident with the recovery of most remaining neurons. Both processes take place during the subacute period, following which the further stages of recovery appear to take place at a slower rate. Occasionally chromatolytic cells may still be found several months after onset of the disease, for example. Similarly, heavily cuffed vessels may persist for at least a year, although such cuffing is gradually reduced markedly after the first six months of the disease. During the late convalescent period, histiocytes also are greatly reduced, and affected regions of anterior horn are characterized by a variable degree of gliosis, which marks the terminal stage of the non-neuronal reparative process.

Some Statistical Findings

A surprising finding in this study was the very high incidence of pathological change in the motor nerve cell population, indicating an almost universal dissemination of virus in the spinal motor cell population in paralyzed individuals. In 40 separate limb regions of 11 animals killed two to five days after onset of paralysis, the percentage of normal cells in motoneuron populations averaged between 3% and 4%. Of these limb regions, seven supplied extremities either clinically normal or showing only mild paralysis, and these showed an average of about 10% of normal motor cells in the total cell populations. Five of these extremities were in animals killed on the fifth day and in which there was no possibility of progression of paralysis. These findings indicate that in some cases, reversible changes may affect the majority of the motoneuron population. Additional strong evidence comes from the finding that whereas normal cells increase from an average proportion of 4% to 50% during the first month after the height of paralysis, destroyed cells do not increase noticeably

during this period. In confirmation of the latter point, moreover, necrotic cells not yet absorbed are negligible in numbers after the third day.

Another important finding concerns the overall mortality of motor nerve cells in relation to the maximal degree of paralysis in the disease. The average proportion of destroyed cells does not vary appreciably after the height of paralysis is reached (two to three days after onset of paralysis). This proportion of the total motoneuron population is about 47% and represents also the grand average of the 120 limb populations examined in this period. Since, on the average, all but 4% of motoneurons are involved in the acute stage, the average proportion of injured nerve cells which are destroyed, or the average "case fatality rate," is almost 50%. The range in our series of cases from the second to the fifth day varies from 12% to 91%. Therefore, one can state that in this series as a whole, there was a 50% probability that an invaded motor nerve cell would be destroyed by viral activity.

Summary

1. Poliomyelitis infection of the CNS consists of a primary invasion of nerve cells and a secondary inflammatory response of variable intensity.

2. The infection of nerve cells may be severely destructive with some strains of the virus or relatively mild with others, and this variation of motoneuron destructiveness or "virulence" is unrelated to the immunological type of the virus.

3. Highest concentrations of poliovirus in the spinal cord are found on the day preceding and the day of onset of paralysis, after which there is a steep decline to extinction of virus between the first and third weeks.[5,6]

4. Peak concentrations of virus are correlated with a diffuse loss of cytoplasmic basophilic substance in almost the entire motoneuron population, irrespective of the severity of the paralysis.

5. Complete loss of basophilic substance, or chromatolysis, is followed by severe nuclear changes and motoneuron destruction, whereas milder degrees of chromatolysis may be followed

by regeneration of basophilic substance, beginning at the cell and nuclear membranes and spreading inward toward the nucleus (central chromatolysis).

6. In many motoneurons showing severe diffuse chromatolysis, one may find intranuclear, acidophilic inclusion bodies of the shape and size of the basophilic nucleolus. These persist into the recovery stage. Whereas in the acute stage they are found only in severely chromatolysed motoneurons, in the later stage they are found in motoneurons in which the basophilic substance is fully regenerated. Thus, the presence of central chromatolysis and of intranuclear acidophilic inclusions in the subacute and convalescent periods is decisive evidence of recovery of motoneurons. This is seen by the end of the first month in almost all surviving motoneurons, although occasional chromatolytic motoneurons may be found as late as several months after onset.

7. Our quantitative studies reveal that poliovirus infection of the spinal cord and brainstem usually involves most of the lower motoneurons, even in those monkeys experiencing relatively mild degrees of weakness.

8. Motoneurons exhibiting only mild degrees of diffuse chromatolysis are probably capable of function. Loss of function appears to be correlated with severe cytoplasmic and nuclear change.

In seeking an explanation for the recurrent weakness of recovered polio patients many years later, one can speculate that recovered motoneurons may be vulnerable for life to metabolic factors such as changes of senescence. For example, Howe and I had shown in 1941 that an intrinsic injury, such as axon interruption of motoneurons, which produce nonlethal chromatolysis, could render the motoneurons resistant to poliovirus during the regrowth phase of the interrupted axon (central chromatolysis). During the first week after axon section, in contrast, the affected neurons are not resistant to virus injection or, indeed, may be more vulnerable than control motoneurons on the opposite side.

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Changes in Spinal Cord Motor Neurons of Possible Relevance to the Late Effects of Poliomyelitis

Prof. B.E. Tomlinson, CBE, MD, FRCP, FRCPath and Dorothy Irving

Introduction

The brunt of the damage to the central nervous system in poliomyelitis occurs in the anterior horns of the spinal cord and, in some instances, the motor cell groups of the brain stem. In many rapidly fatal cases and in many with months or years of survival, the large neurons within the anterior horns, including the gamma motor neurons, are destroyed in many areas. With survival, foci of intense gliosis occur in areas of neuron destruction, leaving within or around them few or many surviving motor neurons according to the degree of damage. Study of the site of focal motor neuron destruction and the muscles which have undergone neurogenic atrophy in survivors has enabled the position and length of the columns of cells in the lumbosacral segments of the cord which supply the various muscle groups and some individual muscles to be determined.[1,2]

Clearly, one possible explanation for delayed deterioration in muscle strength and function in survivors of poliomyelitis with varying degrees of disability would be further loss or dysfunction of those motor neurons which had survived the original attack. This paper looks at the evidence which might be invoked to suggest that loss of motor neurons through increasing age may

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contribute to the delayed deterioration in the disease; to the possibility that immobilization, which on clinical grounds gives rise to rapid deterioration of muscle strength but from which much functional recovery occurs, may also be associated with neuron loss; and at one example of motor neuron damage (limb amputation) which results in delayed loss of the damaged motor neurons, a situation which may be relevant to the study of survivors of poliomyelitis.

Motor Neuron Population of the Human Lumbosacral Spinal Cord

Studies of the total numbers of motor neurons of the human spinal cord have been few. Only the estimate of Alverdes[3] of 100,000 for the whole length of one half of the human spinal cord is given in the 1968 edition of Blinkov and Glezer,[4] though in 1966, Sirkin and Kuhlenberg[5] gave a preliminary estimate of the total numbers in the cord as lying between 80,000 and 160,000. Detailed studies by Tomlinson, Irving and Rebeiz[6] determined, by quantitative analysis, the total numbers of such neurons in the human lumbosacral spinal segments and analyzed the accuracy of various sampling procedures, following initial counting of all nucleolated neurons in serial sections of the whole lumbosacral cord.

In youth, these numbers lie between 55 and 65,000 in all the lumbosacral segments. The numbers in individual segments of the lumbosacral cord[7] were established and the variations in pattern of distribution in the different segments in different individuals; L3 to S1 usually contain over 90% of the total population. Additionally, the variations in numbers on the right and left sides in individual sections were examined as well as the variations from section to section within the same segment. Variations in total numbers of neurons on the right and left sides throughout the whole cord proved to be negligible; in individual heavily populated segments (L2 to S2), variations between left and right sides rarely were as great as 10%, but in individual sections, differences could be threefold, as they could in total numbers between sections at different levels in the same segment. These observations demonstrate clearly the profound errors that can arise from examination of small numbers of sections of the spinal cord, particularly if observations on neuron populations are subjective and not supported by quantitative data.

A quantitative study of the total numbers of limb motor neurons in the human lumbosacral spinal cord from 47 subjects between 13 and 95 years of age[8] showed that below the age of 60 years there was no significant evidence of motor neuron loss, the total numbers of cells lying between relatively narrow limits over this entire period (lowest count 49,807 and highest 65,155 in the 23 patients under 60 years of age). Above 60 years, a considerable and significant mean loss of cells occurred, with increased variation between the highest and lowest counts (Fig. 1). The mean counts per decade are shown in Table 1, where it is obvious that the first significant reduction occurs in the seventh decade. The mean count of the cases in the tenth decade is severely affected by two cases with exceptionally low counts of 31,126

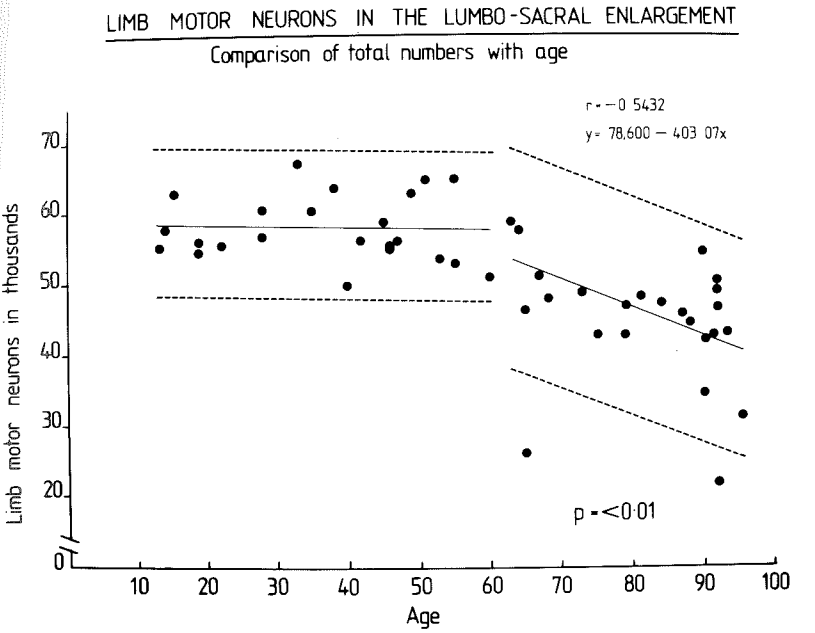

FIG. 1. Numbers of limb motor neurons in the human lumbosacral cord in 47 subjects from 13 to 95 years. The case aged 65 years has been omitted in the calculation of the regression line and the 95% confidence limits (dotted lines) in the group above 60 years.

Table 1. Mean Counts of Lumbosacral Neurons From 2nd to 10th Decades

Age (Years)*	13-20 (5)	21-30 (3)	31-40 (4)	41-50 (6)	51-60 (5)	61-70 (5)	71-80 (4)	81-90 (6)	91-95 (6)
Motor neurons	57,501	57,767	60,171	57,370	57,590	53,456	45,336	45,361	40,691

*Figures in brackets are the numbers of cases examined in each decade.

and 22,218, but illustrates that in extreme old age, occasional cases have lost at least 50% of their original numbers of neurons without being immobilized by muscle weakness or any obvious paralysis. The two cases mentioned above amply illustrate this somewhat surprising fact.

The case with total lumbosacral motor neurons of 22,218 was a 92-year-old man who lived on his own and cared for himself and his flat until three days before his death. He had been physically vigorous and exceptionally well preserved until three months before death when it was noticed that his appetite was failing and he was not caring for himself as well as previously, though he still cleaned his flat, did his own shopping and cooking and had a daily walk. He was found unconscious, hypothermic and dehydrated in his flat, having apparently fallen, though he suffered only minor soft tissue damage. He failed to recover despite gradual return to normal temperature. At autopsy no precipitating cause for hypothermia was found, the only significant finding being a severe suppurative bronchitis. The motor neurons of his lumbosacral cord were diffusely reduced in number, and only one glial star was seen in all the sections examined. There was no evidence of any diffuse glial increase or degenerating neurons, though the majority appeared somewhat small and some of irregular shape, their appearance being dissimilar from the motor neurons of any other case in the series. Samples of his leg muscles showed considerable variation in fiber size with some focal necrosis, but no suggestion of grouped fiber atrophy.

The man with a total motor neuron count of 32,126 died at age 95. He had been a solicitor's clerk and a personal aid to a wealthy American until 86 years of age. He had been alert and

active until three months before his death. He was then admitted to the hospital, depressed and having attempted to commit suicide. He was having frequent attacks of dizziness associated with hypotensive episodes and while in the hospital was reluctant to be mobilized. He was, however, sufficiently fit for day therapy. Careful neurological examination showed no evidence of peripheral or central nervous system disease. The only significant autopsy finding was, again, bronchial suppuration. Apart from the reduced total motor neuron population, the only significant abnormality in the cord was an apparent increase of glial cells within the gray matter. The motor neurons appeared normal to standard histological staining.

One other case from this group is worth comment. A female of 65 years with a total limb motor neuron population in the lumbosacral cord of 25,688 was killed in a road accident while on a shopping trip. She survived in deep coma for 48 hours. She had been medically examined a number of times in the previous five years for respiratory infection and no neurological abnormality had been noted, though the central nervous system had been specifically examined. She had made no complaint of generalized or lower limb weakness. No significant abnormality in the spinal cord was detected beyond the extremely low number of limb motor neurons. These counts were repeated because of the unusually low numbers of motor neurons and a similar count obtained.

These three cases, therefore, illustrate the severe reduction in limb motor neurons which may be found in old people who have retained considerable and apparently entirely normal mobility and physical activity for their age.

Two of these three cases, and all the others in the series, showed motor neurons considered to be of normal appearance for their age by a number of standard staining procedures. Increase in lipofuscin content with increasing age was apparent and resulted in a gradual increase in neuron area on measurement of perikaryon size. But Nissl substance was not obviously diminished though often appearing more powdery than in younger subjects where it assumes the appearance of large granules. Nuclear and nucleolar appearances remained within normal limits. Glial stars and evidence of single motor neuron degeneration were excessively rare. A minor degree of peripheral demyelinization

was apparent in the older cases, as was an increasing number of corpora amylacea mostly in the dorsal columns and subpial white matter. In summary, therefore, this investigation showed a stability in numbers and an apparent normality in appearance of limb motor neurons to the age of 60 years with a variable loss after that time, but with a mean reduction in numbers in the next four decades of some 29%. In the three decades from 60 to 90 years the loss was, however, 21% of the mean count in youth.

It is not possible to compare our findings with any others, since no similar investigation has been found in the literature. However, Kawamura et al[9] in a very detailed examination of 17 cases from 17 to 81 years of age found a reduction of medium and large motor neurons in the anterior horns of the third, fourth and fifth lumbar segments of 18.8% (Fig. 2), this correlating well with the reduction of large and medium sized myelinated fibers in the anterior roots of those segments. This figure is very closely similar to our findings of some 21% over a slightly longer age span. Their restriction of counts to the three most heavily neuronally populated segments makes comparison of total numbers with our findings impossible. Nevertheless, it appears likely that similarly sized neurons were counted in both studies and the most significant difference in the results is that Kawamura et al[9] found evidence of a diminishing population of motor neurons throughout the entire age period investigated. How this discrepancy arises, that is to say, that Kawamura et al recorded a continuous neuron loss with age, whereas we found no significant loss to the age of 60 years can only be a matter of conjecture, but one possible explanation may lie in the significantly smaller number of cases which they examined. It is conceivable that an investigation of a larger number of cases up to the age of 60 years may have revealed less evidence of cell loss over that period, but there is, of course, no certainty of this. Nevertheless, their figures show a loss, between 17 and 60 years of age, of approximately 12.5% an amount, judging from our mobile cases in old age with very great cell loss, which may not have a particularly significant effect on muscle function even in the presence of significant cell loss from previous disease. Our investigation would therefore suggest that in cases of poliomyelitis occurring in early life serious deterioration in muscle function 25 to 30 years later could not be explained by loss of neurons through aging;

and even if cell loss is continuous over the first six decades, cell loss in the remaining normal neurons is small (6% over 30 years) and seems unlikely to be the cause. That statement, however, only has validity if the motor neurons which remain in the spinal cord after an attack of poliomyelitis are normal. Although many accounts of the surviving neurons in the anterior horns after poliomyelitis describe the neurons as "appearing normal," it is our impression on examination of cases of long surviving poliomyelitis that a good many of the surviving neurons are smaller in size. Bodian[10] recorded that patients dying within

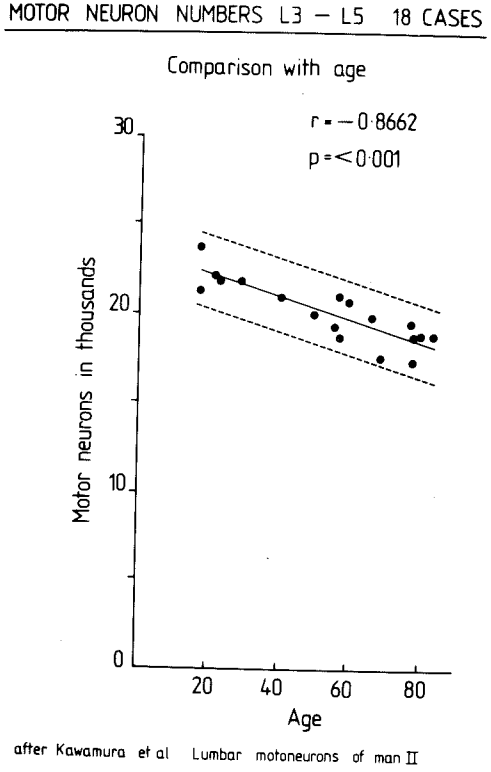

FIG. 2. Numbers of medium and large motor neurons in the third to fifth lumbar segments in 18 cases from 17 to 81 years. (Constructed from the data of Kawamura et al.[9]).

several weeks of an attack show some surviving neurons which are normal and some neurons which are normal apart from the presence of type β eosinophilic inclusion bodies, this appearance being interpreted as indicating that some cells attacked by virus have nevertheless recovered. Clearly, however, any cell invaded by virus is likely to be permanently affected, particularly in relation to protein synthetic mechanisms. It would be imprudent to suggest that such cells would have the same capacity as normal cells to withstand the influence of increasing age as do neurons not so affected.

Effect of Immobilization on Motor Neurons

Although performed for other purposes, investigation of limb motor neurons in patients dying between 15 and 21 years of Duchenne muscular dystrophy[11] and those dying between 48 and 64 years of dystrophia myotonica[12] strongly suggests that severe immobilization over long periods of time has an insignificant effect on limb motor neuron survival. Figure 3 shows the motor neuron counts in five cases of Duchenne dystrophy plotted with the numbers found in normal spinal cords in the same age group. All the counts from the dystrophy cases fell within the normal range and, indeed, the mean count of the dystrophy cases was higher, though not significantly, than the normal controls. Neuron size was also increased, though neuron shape, appearance of Nissl substance, nuclear and nucleolar size and shape all appeared normal in cases in which immobilization had been complete for around 15 years and severely restricted for a somewhat longer period. This fact is even more astonishing when one considers that in the later stages of that disorder, almost all the lower limb muscles have been reduced to minute atrophic remnants embedded in large masses of fat with some excess of fibrous tissue. It would seem impossible for any of the frequently postulated flow of trophic substance from muscle to motor neuron perikaryon to occur under these circumstances. The weakness of the statement that cases of Duchenne dystrophy have normal motor neuron counts after years of total immobilization lies in our ignorance of their motor neuron numbers in infancy. The motor neuron numbers present at death suggest the possibility of a significantly higher level of neuron population if sufficient cases were examined. It is necessary to count the motor neuron

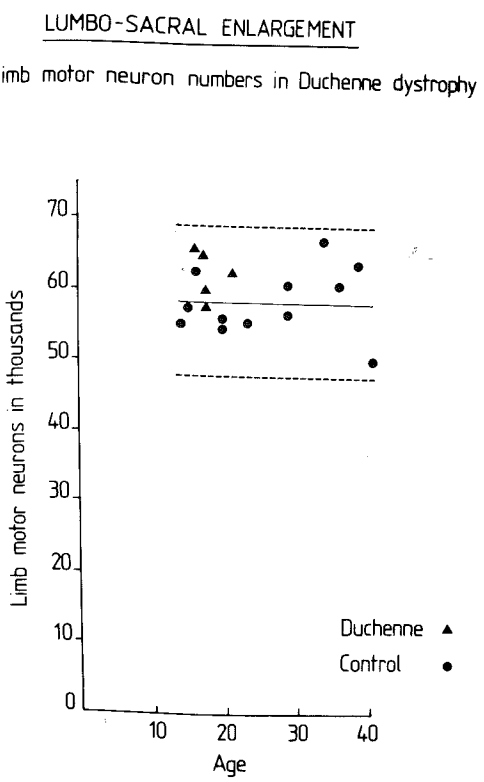

FIG. 3. Numbers of limb motor neurons in five cases of Duchenne dystrophy compared with normal controls of similar age.

population in cases of Duchenne dystrophy in infancy and childhood before firmly stating that their high counts at death eliminate the possibility of motor neuron loss throughout the first two decades. This is particularly so since Sucheela et al[13] have reported an increase of motor neurons in chickens with muscular dystrophy.

Figure 4 shows the limb motor neuron counts in five cases of dystrophia myotonica plotted alongside the motor neuron counts on normal subjects of similar ages. In this disorder severe weakness and disability rather than total immobility occur, but symptoms had been present for between 8 and 22 years before death. Here motor neuron numbers were slightly though not

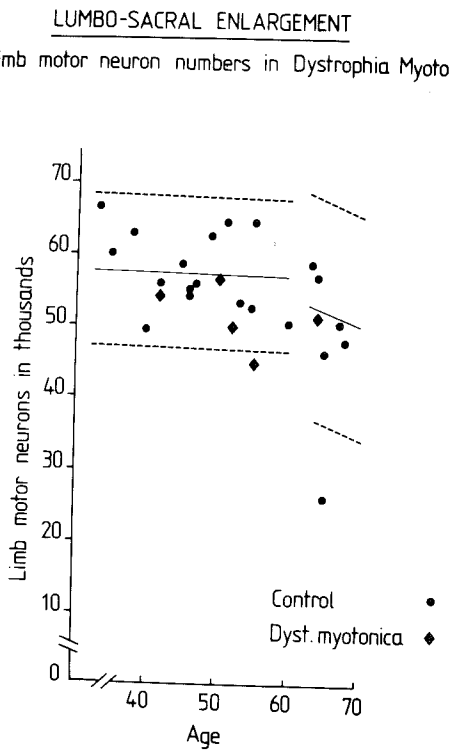

FIG. 4. Numbers of limb motor neurons in five cases of dystrophia myotonica compared with normal controls of similar age.

significantly less than those of normal subjects of similar age. In three of the five cases, the motor neurons were entirely similar in appearance to normal controls. In two cases, however, the motor neurons were small by comparison with normal controls, and in three cases there was an increase in glial cells in the anterior horns, which detailed analysis confirmed was not due to crowding from reduction of volume of the anterior horns as had been found to account for an apparent increase of glial cells in the anterior horns in cases of muscular dystrophy.

Figure 5 shows the motor neuron counts in five cases of total immobilization in a more elderly population due to paraplegia of varying causation, but with lesions involving thoracic or lower cervical cord. Once again the counts fall within normal limits for

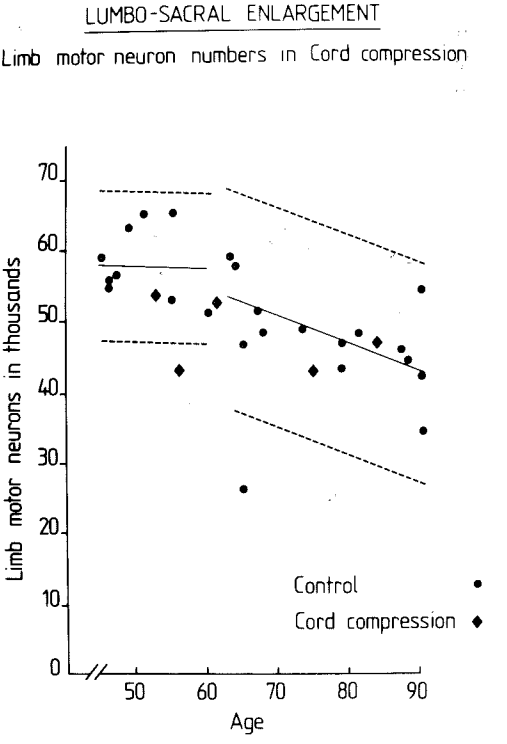

FIG. 5. Numbers of limb motor neurons in five cases of paraplegia from cord compression compared with normal controls of similar age.

the age, and in three cases no significant histological changes were observed in the lumbosacral segments. The period of immobilization was from 4 months to 13 years, the latter case presenting the lowest count in the group but no apparent histological abnormality.

Effect of Neuron (Axon) Damage by Amputation

One other observation of possible relevance to a discussion on late deterioration following poliomyelitis is worth mention. Earlier literature, particularly on experimental axon section, records chromatolysis as a consistent phenomenon in motor neurons. Particularly where axon section has occurred close to

the perikaryon, cytoplasmic vacuolation and eventual death of motor neurons occur. Examination of the human spinal cord following limb amputation has yielded various opinions about the state of the spinal cord, some claims being made that no changes can be observed and others that some neuronal loss and atrophy of the anterior horn eventually occur with decrease in size of remaining motor neurons. Taft[14] in an examination of three spinal cords in cases of amputation drew the conclusion that these could not be distinguished from normal controls of the same age. However, a more recent re-examination of this subject by Kawamura and Dyck[15] reported considerable loss of intermediate and large neurons on the amputated side compared with the nonamputated side in two subjects who had survived 4½ and 9 years after amputation. Our own observations on five cases of lower limb amputation who survived from 3 months to 50 years after amputation (Tomlinson, Irving and Aherne, unpublished data) showed no neuron loss after several months, though numerous neurons showed severe typical chromatolysis with rounding of the neuron body and eccentricity of the nucleus which is characteristic of changes after axotomy. With survival longer than four months (four cases), all cases showed motor neuron loss on the amputated side, the maximum occurring in the cases of longest survival. Even after 50 years, however, considerable numbers of limb motor neurons still showed typical chromatolysis.

The possible significance of this observation is that it illustrates that neurons which have suffered severe damage (in this case, axonal section) may remain in an abnormal state of severe chromatolysis for many years, but with eventual death of many cells, this latter event occurring only very slowly and proceeding for periods as long as 50 years, that is, two-thirds of the average life span. One other possibility arises from this observation on axon section and its eventual lethal effect on the neuron. Neuron loss in poliomyelitis is followed by intense gliosis, commonly with surviving neurons at the periphery and occasionally within the gliosed tissue. Is it possible that surviving neurons, whose axons traverse the gliosed tissue en route to the cord periphery to join the anterior roots, gradually become compressed or distorted so that eventual axotomy occurs? If that were so, cell death would appear more likely than following amputation for the axon

damage would be close to the perikaryon and in neurons possibly already damaged by previous disease. Chromatolysis of some remaining neurons in survivors of poliomyelitis would give some credence to this possibility.

Summary

Normal aging results in diminution in the numbers of motor neurons in the human lumbosacral spinal cord. The mean loss from youth to the tenth decade is around 30%, with increasing differences in individual counts above the age of 60 years by comparison with youth. Subjects in old age with only 50% of motor neurons in youth are nevertheless mobile and physically active to a degree compatible with their age. It therefore seems unlikely that loss of motor neurons from the spinal cord due to normal aging accounts for delayed muscle weakness or increased severity of paralysis in patients who have stabilized physically after poliomyelitis.

Also, motor neurons deprived of normal function so far as stimulation of muscle activity is concerned (as occurs in Duchenne muscular dystrophy) or associated with severe immobilization, as in Duchenne dystrophy, some cases of dystrophia myotonica and in paraplegia from spinal cord compression nevertheless are capable of surviving for many years without gross abnormalities to standard staining procedures.

After severe cell damage such as occurs in amputation, cell death may be much delayed, though it may continue to occur in individual neurons after many years. This finding highlights the fact that damaged neurons may survive for long periods and this may be the position in the spinal cord after an acute attack of poliomyelitis. If damaged neurons do so survive, they may well be more susceptible to cell death with increasing age than are normal neurons.

Clearly, much more detailed and sophisticated investigations of motor neurons in muscular dystrophy and other causes of prolonged immobilization by specialized histological, cytochemical and immunocytological techniques need to be performed before any claim can be made that they are normal. Reinvestigation of material stored from cases of poliomyelitis surviving months or years from the acute attack may yield evidence on the state of

the surviving neurons and may indicate that they are more liable to early death than normal.

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Physiological and Clinical Investigations

Neuromuscular Symptoms in Patients With Old Poliomyelitis: Clinical, Virological and Immunological Studies

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Introduction

Some patients with a past history of acute paralytic poliomyelitis experience not only residual muscle weakness from the initial illness, but also develop, many years later, a slowly progressive muscle weakness.[1-4] The new neuromuscular symptoms may vary in severity from a simple nonprogressive deterioration of function[5] to motor neuron degeneration including muscular atrophy[1,3,4] and forme fruste amyotrophic lateral sclerosis (ALS).[2] The mechanism and frequency of new symptom development in patients with old poliomyelitis are unknown. Possible explanations include reactivation of poliomyelitis virus,[1,2,6] genetic predisposition allowing the previously affected motor neurons to further deteriorate,[2,8] normal aging process in a previously diseased motor unit and reduced ability to compensate for polio-weakened muscles,[2,3,7,9] immunopathologic mechanisms,[4] or merely a simple coincidence.[2]

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In the present study, we examined and clinically classified relatively young patients who, after recovery from acute paralytic poliomyelitis and several years after relative stability, have experienced new neuromuscular symptoms. Seven patients had deterioration of functional capacity without new muscle weakness and ten patients had a slowly progressive, focal lower motor neuron type of weakness that we have termed late-postpoliomyelitis muscular atrophy (late-PPMA).[4] Based on several immunological, virological and histological observations, we suggest that immune mechanisms may play a role in the manifestation of symptoms in some of these patients.

Methods and Patient Selection

Patient Selection

Patients were studied with informed consent by the Infectious Diseases Branch of the National Institute of Neurological and Communicative Disorders and Stroke. Selected patients had a history of acute paralytic poliomyelitis in childhood or earlier adolescence. This was established by a careful review of records insofar as possible to document the clinical occurrence of an acute febrile illness followed by paralysis; by checking for neighborhood or school epidemics; by reviewing the old clinical history with the patient and the family; and by selecting relatively young patients affected in the United States, particularly during the later epidemics between 1945 and 1954 when the diagnosis of poliomyelitis was more accurately made. From all the patients studied, only three had poliomyelitis before 1945: one in 1922, another in 1918 and one in 1930 (Table 1). In addition, all the selected patients fulfilled the following criteria: (1) a partial recovery of motor function and a minimum of a ten-year period of functional stabilization after extensive rehabilitation (most of them in Warm Springs, Georgia) or recovery from corrective surgery; (2) signs of minimal or severe residual neurological damage on neurological examination characterized by muscle atrophy, weakness, arreflexia and normal sensation in groups of muscles with a random distribution; and (3) report of experiencing new neuromuscular symptoms.

All the patients were examined neurologically. Blood

chemistries, CBC, and serum muscle enzymes were determined. Skin tests to common antigens (mumps, candida trichophyton, PPD), were performed on several patients. Patients were excluded if they had a history of diabetes, collagen-vascular disease, exposures to toxic factors, other major viral illnesses or a family history of neuromuscular disease. Seven patients with new muscle weakness and wasting had electromyography and nerve conduction studies and muscle biopsies performed from one of the newly affected muscles processed for muscle enzyme histochemistry as previously described.[10]

Immunological/Virological Studies

The serum and CSF from the patients with new muscle weakness were tested for quantitative immunoglobulins by a nephelometric immunoprecipitation method and for oligoclonal bands using a high resolution agarose gel electrophoresis system as previously described.[11,12] Search for circulating antibodies to neuronal or glia cells was performed by applying the serum to paraffin-embedded spinal cord sections using the indirect immunoperoxidase technique.[13] Peripheral lymphocyte subsets were analyzed as previously described,[14,15] using the following monoclonal antibodies (Ortho, Raritan, NJ) 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 $OKIa_1$ for B cells/monocytes/activated T cells. Viral antibody titers in both serum and CSF were examined by ELISA for measles virus (Edmonston strain) and cytomegalovirus (CMV) as previously described.[16] Antibodies to herpes virus type 1 (McIntyre strain) and type 2 (multiple sclerosis strain), toxoplasma gondii and CMV (strain AD/69) were also examined by indirect hemagglutination inhibition (IHA) technique as previously reported.[17] 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 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 as previously described.[18]

Results

Clinical Classification

From our study of 20 examined patients, 17 of which had new neuromuscular complaints, we distinguished two categories of symptomatic post-poliomyelitis patients (Table 1):

1. A group of seven patients, age 31-62 (average 46 years), had diminished functional capacity and subsequent stabilization without development of new muscle weakness. These patients, most of which had been left with severe disability, had more musculoskeletal than neurological complaints and no progressive muscle weakness. Like the patients described by Anderson,[5] they presented with joint pains, decreased stamina, frequent falling and recurrent injuries, instability of gait and need to a return to bracing or fitting of new bracing. They tended to remain stable for relatively long periods, often at a lower level of functioning or by reducing their work demands. These patients did not experience new muscle weakness or wasting in a defined muscle group after an average period of 37.7 years (range 26-50) from the acute polio and during an average period of 6.4 years (range 3-11) from the time their first musculoskeletal complains had begun.

2. A second group of ten patients, average age 44.3 years, presented with late-slowly progressive post-poliomyelitis muscular atrophy (late-PPMA),[5] characterized by asymmetrical and slowly progressive muscle weakness and wasting, fasciculations and muscle pains. In patients with late-PPMA, who in general had milder residual defect than the previous group, the new symptoms started after an average period of 36.6 years from the acute polio (Table 1) and were limited to lower motor neuron involvement without pyramidal, bulbar or sensory signs. Deep tendon reflexes were absent or diminished and fasciculations were often present. The weakness was characteristically focal (one limb or one side) and, contrary to the previous group, it was very slowly progressive with mild objective and subjective signs of worsening noticeable every one to three years. The late-PPMA distinguished itself from the classic progressive spinal muscular atrophy through its peculiar asymmetrical involvement and probable slower course. The new muscle weakness and atrophy were present in muscles previously weakened by the acute polio or

Table 1. Clinical Characteristics of Late Onset Symptomatology in 17 Patients With Old Paralytic Poliomyelitis

Symptoms (# of Patients)		*Onset of Acute Polio, Year (Age)*	*Extremities Affected*	*Present Age*	*Onset of New Symptoms (Years) After Acute Polio*	*Duration of New Symptoms*
Loss of functional capacity without progressive muscle weakness (7 patients)	1.	1946, (4 years)	4	40	24	2 years*
	2.	1945, (11 years)	4	49	28	10 years*
	3.	1949, (10 years)	4, R, B	48	34	4 years*
	4.	1922, (1½ years)	4	62	58	2 years*
	5.	1948, (19 years)	4 + R	53	24	10 years*
	6.	1952, (9 years)	4, R, B	39	26	4 years*
	7.	1954, (3 years)	4, R	31	22	6 years*
Late-PPMA (10 patients)	1.	1950, (2 years)	2	36	29	2 years
	2.	1918, (10 months)	3	65	55	9 years
	3.	1947, (9 years)	4	43	26	5 years
	4.	1949, (19 years)	4	51	28	4 years
	5.	1947, (5 years)	2	39	31	3 years
	6.	1930, (2 years)	2	54	49	3 years
	7.	1950, (12 years)	2	44	29	3 years
	8.	1950, (3 years)	4	35	30	2 years
	9.	1952, (10 months)	2	30	25	4 years
	10.	1948, (20 years)	4, R, B	50	29	2 years

*Unchanged, without development of new muscle weakness.
+ R: respiratory failure, B: bulbar signs

muscles apparently spared (at least clinically) during the acute disease. In six out of ten cases with late-PPMA, the new weakness was in a group of muscles clinically unaffected by the antecedent polio; in only two of the other four the new symptoms were in muscles segmentally contiguous to the originally affected muscle groups. Pain was a very common manifestation in patients with late-PPMA, and it appeared similar to the pain and muscle cramping that we have observed in the muscles of patients with denervating diseases.[19] This pain, described by some patients as similar to the pain they had experienced during the acute polio, was an intrinsic muscle pain and differed from the skeletal and joint pain often noticed in the first group of patients with diminished functional capacity. Among these late-PPMA patients, none presented with ALS or developed upper motor neuron signs since the onset of their symptoms (average period of five years).

Laboratory and Muscle Biopsy Findings

Blood chemistries, CBC and serum muscle enzymes were normal in all patients except one, patient (#4) with late-PPMA (Tables 1 and 2), who had slightly elevated CPK (500 units, normal up to 180). Electromyographic studies carried out only in the group of patients with late-PPMA showed evidence of neurogenic disease with several giant motor units of amplitude up to 25-30 mV with occasional fibrillations and frequent fasciculations, especially in the newly affected muscles.

Muscle biopsy, performed in seven patients with late-PPMA (Table 2), was taken from a newly affected muscle spared during the initial disease (#1,2,5,6,7) or affected but recovered (#3 and 4). In all the patients, the biopsy was consistent with denervation and reinnervation.[10] Large fiber-type grouping and occasional, scattered small angulated fibers were found with ATPase, NADH, and nonspecific esterase histochemical reactions (Fig. 1). A striking finding, however, was the presence of lymphorrhages (cluster of lymphocytic cells) (Fig. 1) in two patients (#2 and 7, Table 2) or around small capillaries in four patients (#1,2,5,7). In two patients (#2,7) one to two actively phagocytosed fibers were also noted. Generally, no signs of myopathy were evident. Electromyographic or any other needles had not been inserted in the muscles of these patients at least one month prior to biopsy and no recent mechanical injury was reported.

Table 2. Summary of Immune and Viral Studies in Patients with Late-PPMA

Patients	*Lymphocyte Markers*	*CSF Oligoclonal Bands*	*Inflammation in Muscle Biopsy*	*Antibodies to Poliovirus in the CSF*	*Antineuronal and Glia Cell Antibodies*
1	OKT4/OKT8 3.7:1,*	4 Bands	Lymph. infiltrates	Negative	Negative
2	OKT4/OKT8 0.86:1,*	2 Bands	Lymphorrhages	Negative	Negative
3	OKT4/OKT8 1.3:1,	Not done	None	Negative	Negative
4	OKT4/OKT8 3.1:1,*	Not done	None	Negative	Negative
5	OKT4/OKT8 2:1,	?	Lymph. infiltrates	Negative	Negative
6	OKT4/OKT8 0.28:1,*	3 Bands	None	Negative	Negative
7	OKT4/OKT8 4:1,*	?	Lymphorrhages	Elevated	Negative

*Abnormal ratios (normal 1.8 ± .05)
? = equivocal demonstration of very faint bands.

FIG. 1. Frozen section of a muscle biopsy from patient with late-PPMA stained with modified trichrome. Muscle specimen, taken from previously unaffected muscle, shows lymphocytic response around vessel and small angulated fibers indicative of active denervation.

Immunological and Virological Studies

Analysis of lymphocytes with monoclonal antibodies was performed in all the patients from the two groups and in an additional three totally asymptomatic post-polio patients. The markers for lymphocyte subsets and OKT4/OKT8 ratio (Fig. 2) were normal in all the patients of the first group except one (#3). The three asymptomatic post-polio patients also had normal lymphocyte subsets. Several alterations, however, were noted in their lymphocytic subsets and OKT4/OKT8 ratio (Fig. 2) in patients with late-PPMA. One patient (#6) had a very low number of cells with helper markers with increased number of cells with suppressor markers and reversed OKT4/OKT8 ratio. Four patients (#1,4,7,10) had an increased OKT4/OKT8 ratio due to a simultaneous slight decrease in number of cells with suppressor

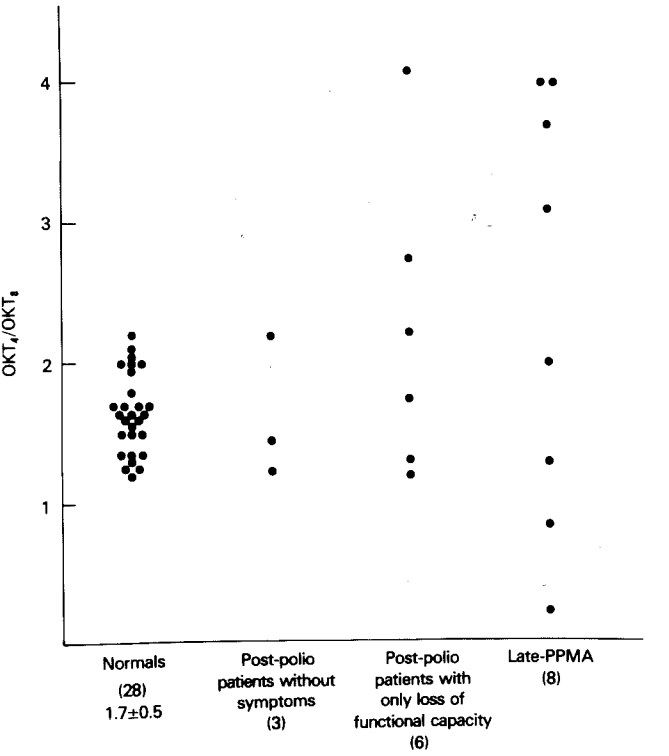

FIG. 2. Analysis of lymphocytes with monoclonal antibodies and the OKT4/OKT8 (helper/suppressor) ratio in normals and post-polio patients. Patients with late-PPMA have increased incidence of abnormal OKT4/OKT8 ratio in comparison to normals and other post-polio groups.

markers and a slight increase in the number of cells with helper markers.

Search for antibodies to CNS cell components failed to reveal specific binding to neurons, glial cells or vascular endothelial cells in all the patients. Spinal fluid analysis for oligoclonal bands revealed the presence of two to four bands in three patients with late-PPMA (#1,2,6) (Fig. 3). This is in contrast to the CSF of patients with classic ALS, where no bands have been seen. Unfortunately, CSF from asymptomatic post-polio patients or from our first group was not available.

Polio plaque neutralization antibody titers measured in six patients in both serum and CSF appear in Table 3. When the BBB permeability was corrected,[18] one patient (#7, Table 2) had high titers to the poliovirus in the spinal fluid; these titers were high for all three types of poliovirus although this patient was never immunized for polio. Antibody titers to other viruses were not different from normals in all the patients.

Discussion

From the study of 17 patients with prior poliomyelitis referred to us with new symptoms, we distinguished two groups of patients with different symptomatology. One group of seven patients had musculoskeletal symptoms causing diminished functional capacity but not new muscle weakness. They remained stable after readjusting their braces or work habits. The other group of ten patients had signs of a new motor neuron disease that we have termed late progressive post-poliomyelitis muscular atrophy (late-PPMA)[4] characterized by slowly progressive focal and asymmetrical muscle weakness of lower motor neuron type occurring in either new muscle groups previously spared or muscles that had previously recovered. This new muscle weakness was very slowly progressive, suggesting that late-PPMA is a rather benign form of motor neuron disease. Although ALS or an ALS-like picture has been suggested to occur late in life among survivors of old poliomyelitis,[2,6] none of the small number of patients that we studied developed upper motor neuron signs during an average period of 4.5 years from the beginning of their new symptoms.

The mechanism of the new progressive muscle weakness in patients with old poliomyelitis is uncertain. In contrast with the other motor sensory diseases, poliomyelitis is an acute anterior horn cell disease in which a substantial recovery occurs, especially in non-severely weakened muscles, when a sufficient number of anterior horn cells survive. When anterior horn cells die, denervation ensues accompanied by reinnervation and sprouting of terminal axons from neighboring healthy motor neurons (Fig. 4) that now supply a larger number of muscle fibers, control a greater than normal percentage of muscle function, and have greater metabolic demands. Because the aging process affects the viability of the motor neurons[20,21] and the ability of their axons

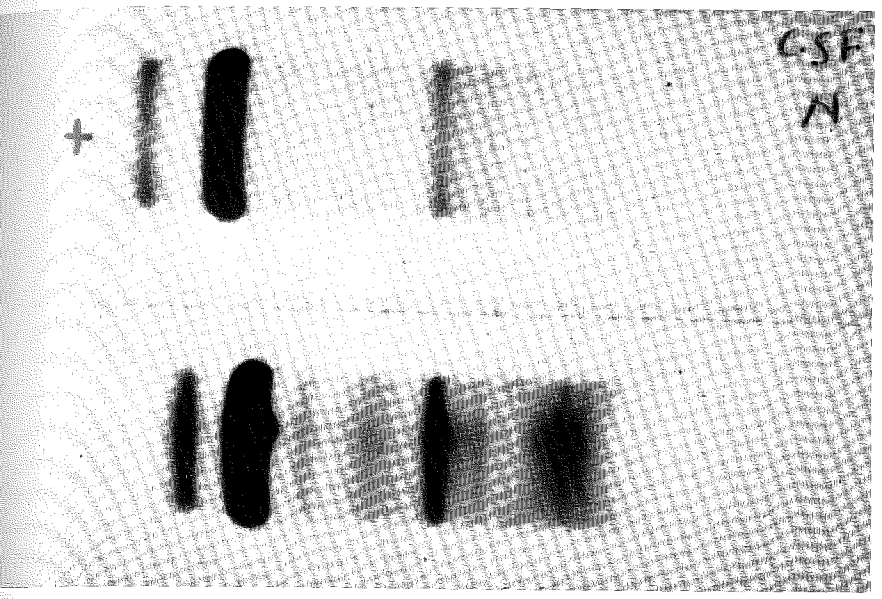

FIG. 3. Agarose gel electrophoresis of spinal fluid from normal control (top gel - N) and patient with late-PPMA (bottom gel). Four oligoclonal bands are seen in the IgG region in patient with late-PPMA.

to sprout, "overworking" anterior horn cells may succumb earlier to the aging process, producing noticeable clinical weakness in patients with old poliomyelitis (Fig. 4). Furthermore, some of the previously affected neurons that escaped death have remained in a borderline or below normal state of functioning and, after a certain period, cannot maintain the metabolic demands of the periphery, resulting in "dying back" axonopathy of their sprouting axons (Fig. 4). When these processes occur in segmentally contiguous neuronal groups, "new" muscle weakness is clinically more noticeable because the succumbing neurons were responsible for a greater than normal percentage of muscle function. Although these possibilities can reasonably explain the new weakness that occurs in already weak muscles and those segmentally contiguous to muscle groups with maximal involvement, they are not sufficient to explain the young age of patients who developed late-PPMA and the development of new weakness in muscles previously spared during the acute disease (even though

Table 3. Polio Plaque Neutralization Antibody Titers

	Polio 1			*Polio 2*			*Polio 3*		
Patient Late-PPMA	*Serum Titer*	*CSF Titer*	*CSF Serum X10³*	*Serum Titer*	*CSF Titer*	*CSF Serum X10³*	*Serum Titer*	*CSF Titer*	*CSF Serum X10³*
1	61,162	55.0	0.90	2,185	<4.0	-	1,547	<4.0	-
2	3,728	8.3	2.23	1,339	<4.0	-	464	<2.0	-
3 ND									
4	11,654	8.9	0.76	1,160	<2.0	-	< 64	<2.0	-
5	4,410	3.0	0.68	434	<4.0	-	2,484	4.6	1.85
6	53,270	92.6	1.74	976	<4.0	-	< 64	<2.0	-
7*	1,034	21.2	20.50*	5,841	138.0	23.63*	3,072	36.7	11.95*

ND = not done
*High CSF titers

Neuromuscular Changes in Patients with Old Poliomyelitis

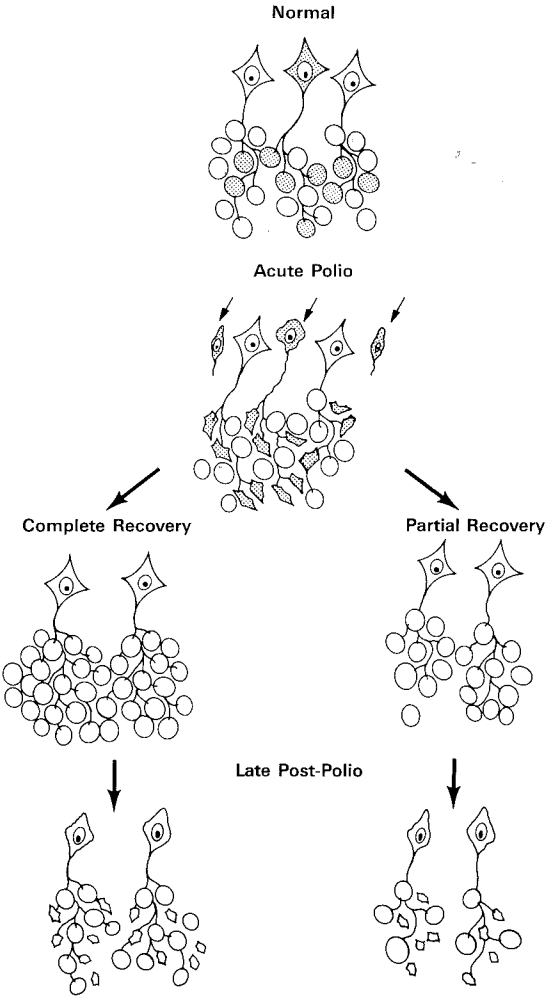

FIG. 4. Diagrammatic changes in the motor units of patients after acute polio and immediate recovery and many years later (post-polio). Death of anterior horn cells after acute polio is followed by complete or partial recovery by reinnervation and sprouting of the terminal axons from neighboring healthy motor neurons which now supply a larger number of muscle fibers. These "overworking" anterior horn cells may succumb earlier to the aging process resulting in noticeable weakness (late post-polio) because they control a greater than normal percentage of muscle function.

they may have been subclinically affected) or in muscles remote from the previously weak ones. For example, three of our patients (#1,6,7, Tables 1 and 2) with mild acute polio affecting only the lower extremities had now developed new symptoms demonstrated clinically, electrophysiologically and histologically in one of the upper extremity limbs. This raises the suspicion that a new or extended disease process may be taking place and other explanations are needed.

From the seven late-PPMA patients that we further studied, four had an inflammatory cellular reaction (lymphorrhages or lymphocytic infiltrates) in the muscle biopsy, three of three studied had oligoclonal IgG bands in the spinal fluid, five had variable abnormalities in the T lymphocyte subsets and one had increased production of antibodies to poliovirus in the CSF (Tables 2 and 3), suggesting that immunopathological mechanisms are active and may be responsible for the manifestation of symptoms in some of those patients.

Lymphorrhages have been noted occasionally in the muscle biopsies of patients with myasthenia gravis, an autoimmune disease, but they are not seen in the muscles of patients with motor neuron disease. Their presence along with lymphocytic infiltrates in the muscle biopsies of patients with late-PPMA may indicate cell hypersensitivity or involvement of cell-mediated immune mechanisms. Although alterations in the lymphocyte subpopulations noted in some of the late-PPMA patients may indicate abnormal immunoregulation, these changes were variable and their significance is at the moment unknown. The presence of IgG bands in the spinal fluid suggests antibody response to an antigenic stimulation in the CNS. Such IgG bands have been seen, for example, in patients with SSPE, representing an antibody to measles, and in multiple sclerosis, representing antibody response to unknown antigens.[11,12] They have not been seen in patients with motor neuron diseases.[11] In our patients with late-PPMA, these bands were weak and associated with normal IgG in the spinal fluid, indicating a weak antibody response to an antigenic stimulus. Whether these bands have been present since the acute infection 30-40 years ago or represent an antibody response to poliovirus and neuronal proteins remains to be determined. Search

for antineuronal or antiglia cell antibodies was negative in these patients' serum.

The presence of mild immunological dysfunction in some of the patients with late-PPMA raises the suspicion of an ongoing dysimmune process which theoretically could facilitate reactivation of the poliomyelitis virus or be caused by it. Poliomyelitis virus, an RNA virus, is usually cytolytic; however, it can cause a persistent infection in animals and immunosuppressed humans.[22-24] Mice intracerebrally inoculated with the Lansing strain of poliovirus type 2 develop prolonged infections up to 77 days at low levels of infectivity[22] and Theiler's virus, a mouse picornavirus similar to human type 2 poliomyelitis virus, can produce acute encephalitis followed by late progressive demyelination.[23] The presence of neutralizing antibodies may be important in establishing such persistent enterovirus infection.[25] Because local CNS infection with poliovirus can stimulate antibody production within the CNS without evidence of serum antibody production,[26] and our late-PPMA patients have been exposed to the natural infection and possibly to the widespread use of killed or attenuated vaccines, determinations of serum antibody titers alone are not sufficient to indicate persistent infection. In our patients with late-PPMA, we looked for antibodies to poliovirus 1, 2 and 3 in both serum and CSF and determined the local antibody production to poliovirus in the CSF by correcting the titers for differences in the BBB permeability (Table 3).[18] Only one of the late-PPMA patients had high titers to poliovirus in the CSF, and this elevation occurred with normal BBB and normal serum and CSF IgG. Although in this patient the antibody titers in the CSF were high for all three types of poliovirus, this elevation was specific for polio and not for the other viruses tested. For example, the antibody titers to measles were 1280 in the serum but negative in the CSF. This patient was never immunized for polio, but she gave a history of polio and exposure to two children with acute polio. It is not known, at the moment, whether the high antibody titers to poliovirus indicate persistent infection in this patient. The CSF is now being retested for poliovirus antibodies using other techniques, including ELISA and radioimmunoassay.

Summary

New lower motor neuron disease distinct from ALS in course and prognosis can occur in patients with old poliomyelitis even in previously spared muscles or muscles remote from the previously affected areas. Although the pathogenesis of this new disease is unknown, immune mechanisms may play a role. Whether a persistent viral infection is involved remains to be determined. Further studies are needed to substantiate these observations with a larger number of patients and define the frequency of new muscle weakness among survivors of old poliomyelitis.

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Pathophysiology and Late Changes of the Motor Unit After Poliomyelitis

David O. Wiechers, M.D.

Introduction

Polio had a direct effect upon the motor neuron, and many motor neurons were unable to survive. Others, however, were capable of recovering given adequate time. The motor neuron is a portion of the motor unit. The motor unit is the building block of the neuromuscular system and consists of the motor neuron, its axon and all of the individual muscle fibers innervated by that motor neuron. With the death of the motor neuron in polio, Wallerian degeneration occurs in the axon and in the presynaptic portions of the end plate. This results in a loss of trophic influence to the muscle fiber. These muscle fibers subsequently develop receptor sites to acetylcholine along their surface membranes.

No longer maintaining a stable resting membrane potential, these muscle fibers spontaneously discharge or fibrillate. The orphaned muscle fibers are capable of sending a distress signal by some unknown mechanism to neighboring motor units that are still functioning. These functioning motor units then respond by sending axon sprouts toward that muscle fiber. Where this sprout comes in contact with the free fibrillating muscle fiber, a new neuromuscular junction forms. If there are no functioning motor units nearby, the muscle fibers fibrillate and atrophy until they die.

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The reinnervated muscle fibers are connected to their new parent motor neuron by very immature terminal axon sprouts. Transmission from the axon to the new terminal axon sprout is initially tenuous, and conduction in the unmyelinated terminal axon sprout is slow. This new neuromuscular junction is also immature and another site of transmission failures. Over a period of four to six months, maturation occurs in the terminal sprouts and the neuromuscular junction, and transmission of the impulse within the motor unit becomes normal. The result of reinnervation by terminal axon sprouting is a motor unit that is comprised of more muscle fibers than normal. When there is a large overall loss of motor units in the muscle, the muscle is usually weak because not all of the fibrillating fibers can be reinnervated.

Return of strength in poliomyelitis is the result of three processes: (1) motor neurons that were initially affected but recovered and regained function; (2) reinnervation by functioning motor units of muscle fibers that were left orphaned by the death of their motor neuron; and (3) strengthening of the remaining functioning muscles by exercise.

Single Fiber Electromyography Studies

In an attempt to study the physiology of the reinnervated motor units in polio, several new neurophysiologic techniques have been employed. Single fiber electromyography is a technique that was developed to study variability of impulse transmission within a single motor unit. This technique involves the recording of a single muscle fiber discharge by an electrode with a 25 micron diameter recording surface. With this technique one can record the variability of neuromuscular transmission between two muscle fibers that belong to the same motor neuron.

Over the past several years, we have been using this technique to study the physiology of the large reinnervated motor units of poliomyelitis patients. We have found that transmission of electrical impulses within large reinnervated motor units of most post-polio patients is abnormal. There appears to be abnormal variability in the capacity of the motor neuron to transmit the impulse to all of its pathologically increased numbers of muscle fibers. In many motor units, transmission fails or is blocked with repetitive discharge. This study reveals an almost linear relation-

ship between the years since recovery from poliomyelitis and the increased variability of neuromuscular transmission. There is also a direct and linear relationship between time since recovery from poliomyelitis and the percentage of motor units with failed transmission to individual muscle fibers.

It is not known specifically if the site of transmission abnormality is pre- or post-synaptic. Transmission during recording, however, is improved by having the patient rest for as little as a few seconds. Tensilon studies to date are inconclusive.

One explanation for the increase in fatigue and weakness in older polio patients may be the progressive blocking or dropping out of individual muscle fibers with repetitive discharge of a motor unit. From these studies, we are led to conclude that the motor unit originally designed to drive 100 or 500 muscle fibers, which now is forced to drive 1,000 to 2,000 muscle fibers, may develop difficulty transmitting impulses to every muscle fiber after 20 to 30 years. The etiology of these transmission failures is unknown, but most likely related to the inability of the motor neuron to meet the metabolic demands of every muscle fiber in its motor unit with increasing age.

Possibly, the motor unit is undergoing peripheral disintegration. If the motor unit is dropping off some of its muscle fibers, some short-duration polyphasic potentials would be expected on electromyographic recordings, as is frequently seen in a myopathy. However, small motor units are not observed in polio.

Macroelectromyography Studies

Possibly the reinnervated motor unit is losing muscle fibers until it reaches its original size. To study this concept, the technique of macroelectromyography was employed. Macroelectromyography is another advanced neurophysiologic technique to study the physiology of the whole motor unit. A very large surface electrode is used to record the depolarization of every muscle fiber that belongs to one motor unit. This requires digital averaging and other electronic techniques.

During the year that we have been using this technique to study post-polio muscles, we have made several observations. The most striking finding was the low number of individual motor units actually present in many of the muscles that were of an-

tigravity strength. In muscles that were a grade F or 2/5, it became difficult at times to find 20 different motor units within the entire muscle.

To date, nine subjects have been studied; with this small sample, no definite conclusions can be made. However, certain observations have been made. We have not recorded any motor units in our polio patients that were smaller than normal size. The patients to date who have recently recovered from poliomyelitis seem to have a greater percentage of the extremely large reinnervated motor units. Rarely did we observe a normal-size motor unit. The patients, however, who were furthest post-recovery seemed to have a greater percentage of normal-size motor units. This implies that our hypothesis that individual muscle fibers per motor unit are lost with advancing age in these reinnervated motor units after polio may, indeed, be correct.

Further studies of these and additional patients as they age will hopefully give us further information regarding the pathophysiology of the reinnervated motor units after poliomyelitis.

Discussion

The questions that now present themselves are more perplexing. If this process of motor unit transmission fatigue and peripheral disintegration is occurring in the reinnervated motor units of all old polio patients, why do only a few patients develop progressive muscular atrophy? Single fiber studies of the aging demonstrate these same abnormalities of motor unit transmission occurring to a milder degree in subjects older than 60 years. Could these neurophysiologic abnormalities represent a more rapid, but natural aging process? Could the overuse of muscle with physical activity accelerate the process? Could the chronic contraction of muscle to handle the tension and stresses of midlife be the major factor that determines who becomes symptomatic? These issues as well as those of pathophysiology must certainly be addressed to gain insight into this problem.

Motor and Sensory Functioning With Changing Ambient Temperature in Post-Polio Subjects: Autonomic and Electrophysiological Correlates

Richard L. Bruno, Ph.D., Julia C. Johnson, M.S. and William S. Berman, M.D.

Introduction

It has long been appreciated that post-polio patients experience a profound decrease in the temperature of their affected limbs with exposure to even mildly cold ambient temperatures. This decrease in limb temperature is associated with often severe burning pain, hyperesthesia and color changes, which range from cyanosis and mottling[1] to "a blend of violet color varying from reddish violet to a deep dark blue violet."[2] Both the coldness of the limbs and pain are tenacious; hours of warming are required to raise limb temperature and relieve pain.[3] Recently, post-polio patients have reported that both manual dexterity and muscle strength decrease noticeably with cold exposure and that all cold-related symptoms become more pronounced with aging.

It has been hypothesized that the cold-related decreases in limb temperature are produced by an underlying "vasospastic sympathetic hyperreflexia."[3,4] The histologically demonstrated damage to intermediolateral column sympathetic neurons following polio virus infection[4,5] has been thought to reduce descend-

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ing inhibition of sympathetic outflow in post-polio patients. This hypothesized release of sympathetic inhibition would increase tonic sympathetic vasoconstrictor outflow and allow even mild "normal stimuli, particularly cold"[3] to produce exaggerated vasospasm and the marked and lasting decreases in limb temperature.

The literature provides little support for this hypothesis. Abramson et al[6] failed to find consistently lower skin temperature or muscle blood flow in the affected limbs of post-polio patients at thermoneutral ambient temperatures. Stenport[2] noted that an affected lower extremity that was cold at the end of the day was often actually warmer than the unaffected extremity upon arising in the morning. These findings do not indicate the presence of tonic vasospasm in post-polio patients. The description of the violet hue of affected extremities during cold exposure and dependency is actually indicative of passive venous dilatation and not arterial vasoconstriction. Further, the scattered distribution of damage to both pre- and post-ganglionic sympathetic neurons[4] should *decrease* sympathetic vasoconstrictor outflow from the affected segments and not release descending inhibition as would a circumscribed suprasegmental spinal cord lesion.[7]

Because of the contradiction between the "vasospastic sympathetic hyperreflexia" hypothesis and both clinical and empirical observations, this study was undertaken to document autonomic vasomotor activity and sensory, motor and peripheral nerve functioning during cold exposure in post-polio patients.

Methods

Subjects

Post-polio subjects [mean age: 48 years (range: 31 to 65 years); five females, one male] and age-matched controls (n = 5) were studied. Post-polio subjects reported significantly greater involvement in the left arm and hand (10% - 50% of full function) as compared to the right (45% - 95%). All reported impaired manual dexterity and markedly cold upper extremities, pain and/or hyperesthesia with exposure to decreased ambient temperature (T_a). Subjects were free from diabetes, other neurological, cardiovascular and peripheral vascular disease and were not taking medications at the time of the study.

Autonomic Measures

Digital cutaneous blood flow was recorded bilaterally using two Hokanson EC-3 strain gauge plethysmographs,[8] which were interfaced with a Wescan rectilinear chart writer. Mercury-in-silastic strain gauges were applied around the center of the most distal segment of the index finger of each hand. Venous occlusion was not employed in the measurement of blood flow because it was considered vital that normal venous outflow not be impeded. An index of blood flow was employed that used the percentage change in digital pulse volume divided by the R-R interval to quantify pulsatile flow in ml/100 mg of tissue/minute.[9] Temperature was measured using a Yellow Springs 4S-3 thermistor thermometer. A thermistor was taped over the distal crease of the volar aspect of each wrist to measure near median nerve temperature [10] and one was placed at the level of the board on which the hand function tests were performed to measure T_a.

Electrophysiological Measures

Median nerve distal motor onset latencies, sensory peak latencies and nerve potential amplitudes were measured bilaterally with a Cadwell 7200 electromyograph using standard technique.[11] Orthodromic motor nerve stimulation was performed across a distance of approximately 8 cm between a bar electrode placed over the volar aspect of the wrist (between the palmaris longus and flexi carpi radialis tendons) and one placed over the muscle belly of the abductor pollicis brevis (APB). Antidromic sensory nerve stimulation was performed across a distance of approximately 14 cm between the wrist bar electrode and ring electrodes placed on the index finger at the proximal and distal interphalangeal joints. Ground electrodes were placed on the palms. Stimulus duration was 0.1 msec and stimulus intensity was varied from 0.0 mA to the point at which a supramaximal response was elicited.

Subjective Rating of Electrical Stimulus Intensity

During the application of electrical stimuli for the measurement of the electrophysiological parameters, subjects were asked to rate the perceived intensity of each stimulus on a zero to ten scale, with zero being "no sensation" and ten equalling "the most

intense sensation ever experienced."[12] Intensity ratings were requested during the sensory nerve measurements to familiarize the subjects with the stimulation and rating procedures. The ratings obtained during motor nerve measurements were recorded for each hand, regressed on the electrical stimulus intensity (in mA) and averaged across subjects. The slope of the regression line represented the sensitivity of the subjects to the electrical stimuli, while the x-axis intercept indirectly indicated the stimulus detection threshold.

Hand Function Testing

Four subtests of the Jebsen Hand Function Evaluation[13] were administered in the following order: subjects manipulated small common objects (placed two, one-inch paperclips, two bottle caps and two pennies in an empty one-pound coffee can), stacked four plastic checkers, and moved five empty #303 cans (large light objects) and then five full #303 cans (large heavy objects) from the table onto the testing board. Each individual task was performed first with the right and then with the left hand. Task completion time was recorded for each hand and the subjects were videotaped during task performance so that prehensile patterns could be evaluated.

Procedure

Subjects were instructed not to smoke or consume caffeine-containing foods or beverages from 12 hours prior to testing. Testing was performed in a temperature-controlled room (Hot Pack, Philadelphia). Each subject was clad in a short-sleeved shirt and sat in a wheelchair at an adjustable-height table to which the hand function testing board was attached. Informed consent was obtained, and the subjects' forearms were supinated and rested comfortably on foam pillows placed on the table. The skin was cleaned with 70% isopropyl alcohol and electrodes, then strain gauges and thermistors were applied.

Ambient temperature (T_a) was set at 25 °C and skin temperature (T_s) was recorded at minute intervals. When T_s was constant bilaterally for five minutes, three minutes of baseline cutaneous blood flow was recorded. At 25 ° only, subjects were asked to subtract sevens serially from 300 to elicit the cutaneous

vasoconstrictor response to mental arithmetic stress. Right, then left median sensory and right, then left median motor nerve conduction parameters were measured. At this point, all transducers and electrodes (except for the wrist and APB bar electrodes) were removed, the hands were cleaned with alcohol and the hand function tests were administered. Electrodes and transducers were then reapplied and the procedure was repeated with T_a set at 30 °C and finally with T_a at 20 °C. This temperature exposure sequence was employed to control for the effects of practice on hand function test performance with repeated testing.

Data Analysis

Nonorthogonal analysis of variance (ANOVA) was applied to examine the effect of temperature on the parameters measured and to compare differences between hands within the two subject groups. Split-product ANOVA was employed to examine the effect of temperature while comparing differences between hands across the two subject groups. Only F values that reached the $p<0.05$ level of significance have been reported.

Results

Autonomic Measures

There were significant bilateral decreases in cutaneous digital blood flow with decreasing T_a in both the post-polio patients ($F=21.8$; $p<.001$) and controls ($F=18.6$; $p<.001$) (Fig. 1). Blood flow was significantly lower in the left (more affected) hand as compared to the right hand of the post-polio subjects at 30 °C ($F=5.9$; $p<.049$) and as compared to the left hand of the controls at both 30 °C and 25 °C ($F=9.1$; $p<.019$). There was no significant difference in blood flow between the two hands at any temperature in the controls or between the two groups at 20 °C. There was also no significant difference between the hands or between the two groups with regard to the percentage decrease in blood flow with cooling from 30 °C to 20 °C, which ranged from 74% to 78%. However, post-polio subjects did not show the 25%-50% decrease in cutaneous blood flow which is normally seen during mental arithmetic; post-polio subjects responded with blunted vasoconstriction (0.0% - 27%) or marked vasodilatation (8% - 95%).

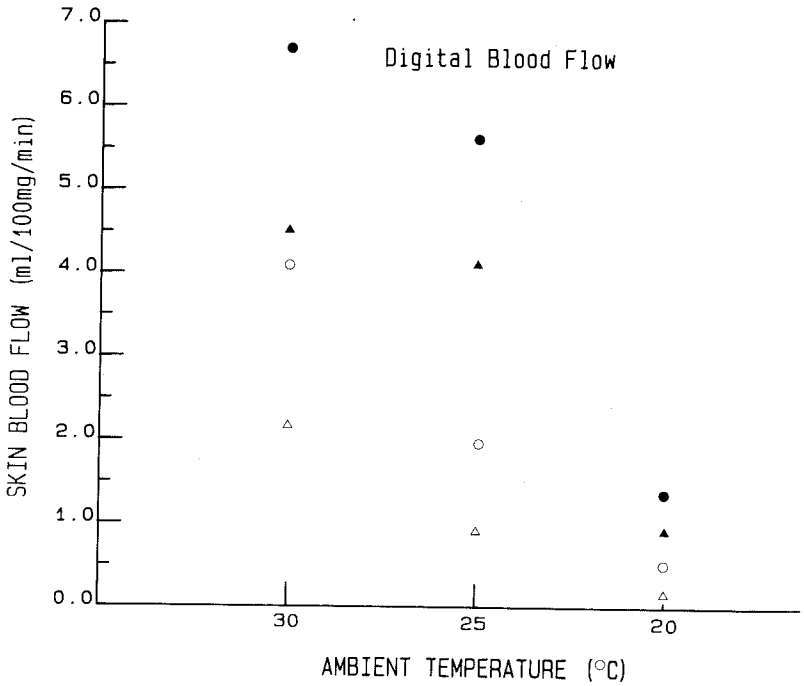

FIG. 1. Cutaneous digital blood flow measured at each ambient temperature. Δ: Post-polio subjects, left hand; ○:Post-polio subjects, right hand; ▲:Controls, left hand; ●:Controls, right hand.

There were significant bilateral decreases in near nerve skin temperature with decreasing T_a in both the post-polio subjects ($F = 28.4$; $p < .001$) and controls ($F = 89.8$; $p < .001$) (Fig. 2). However, there was no significant difference in T_s between the hands or between the two groups at any T_a.

Electrophysiological Parameters

There were significant bilateral increases in median motor nerve onset latency with decreasing T_a in both the post-polio patients ($F = 5.7$; $p < .029$) and controls ($F = 27.8$; $p < .001$) (Fig. 3). Median sensory nerve peak latency also increased bilaterally with decreasing T_a in both the post-polio patients ($F = 5.6$; $p < .014$) and controls ($F = 6.9$; $p < .007$) (Fig. 4). There were no signifi-

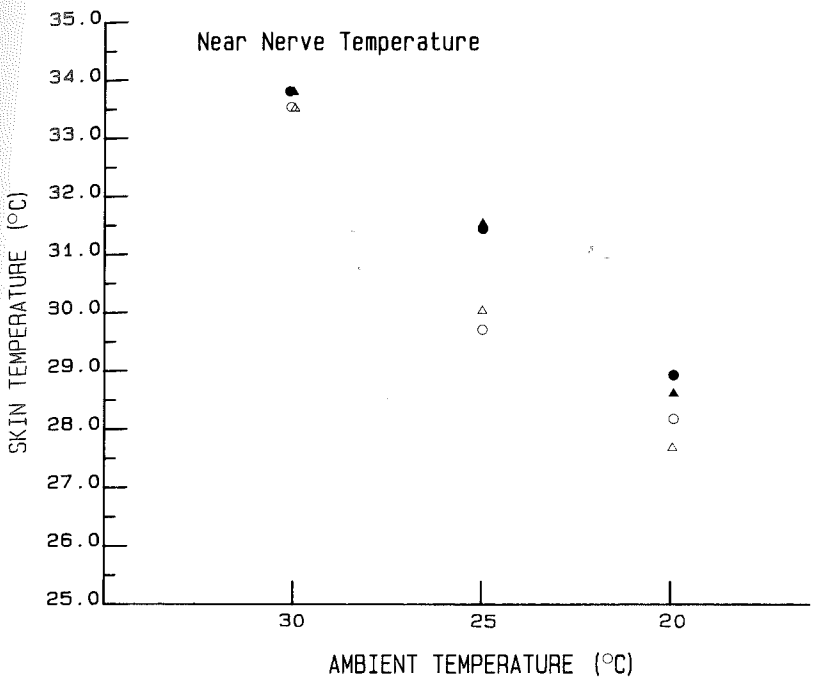

FIG. 2. Near median nerve skin temperature at each ambient temperature.

cant differences in motor or sensory latencies between the hands or between the two groups at any T_a. However, at 25 °C, motor latencies were clinically abnormal (>4.3 msec) in the more affected hand of three (60%) of the post-polio subjects. At 20°, motor latencies became clinically abnormal in the more affected hand in four (80%) and in the less affected hand in three (60%) post-polio patients. Sensory latencies also became clinically abnormal (>3.6 msec) bilaterally in two (40%) of the post-polio patients at 20 °C.

Motor potential amplitudes were significantly lower (64%-90%) in the left ($F = 48.1$; $p < .001$) and right ($F = 21.8$; $p < .001$) hands in the post-polio subjects as compared to the controls, but there was no effect of T_a on motor potential amplitude in either group. In contrast to the motor amplitudes, sensory potential amplitudes did increase significantly in the post-

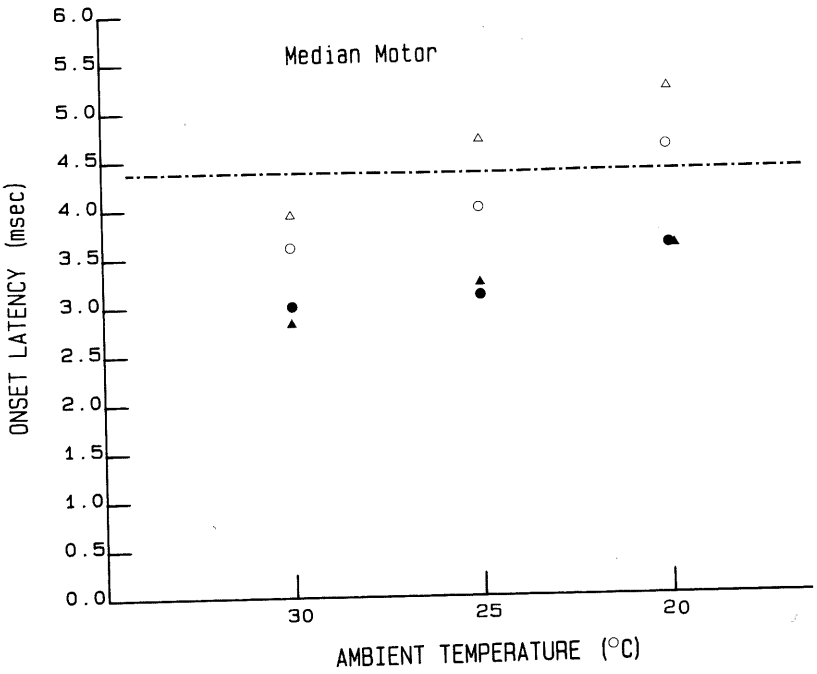

FIG. 3. Median motor nerve onset latency at each ambient temperature. Dashed line marks the upper limit of normal range (4.3 msec).

polio subjects ($F = 7.6$; $p < .005$) and in the controls ($F = 9.1$; $p < .002$) as T_a decreased (Fig. 5). "Giant" sensory potentials (>80 uV) were seen on the more affected side in two (40%) of the post-polios at 25 °C and in three (60%) at 20 °C (cf. Ginzburg et al[17,18]).

Subjective Rating of Electrical Stimulus Intensity

There were no significant differences in the current threshold for detecting the electrical stimuli between the hands or between the two groups, nor was there a significant difference in sensitivity to the electrical stimuli between the hands in either group. There was no significant effect of T_a on threshold or on sensitivity in either group. However, post-polio patients were significantly more

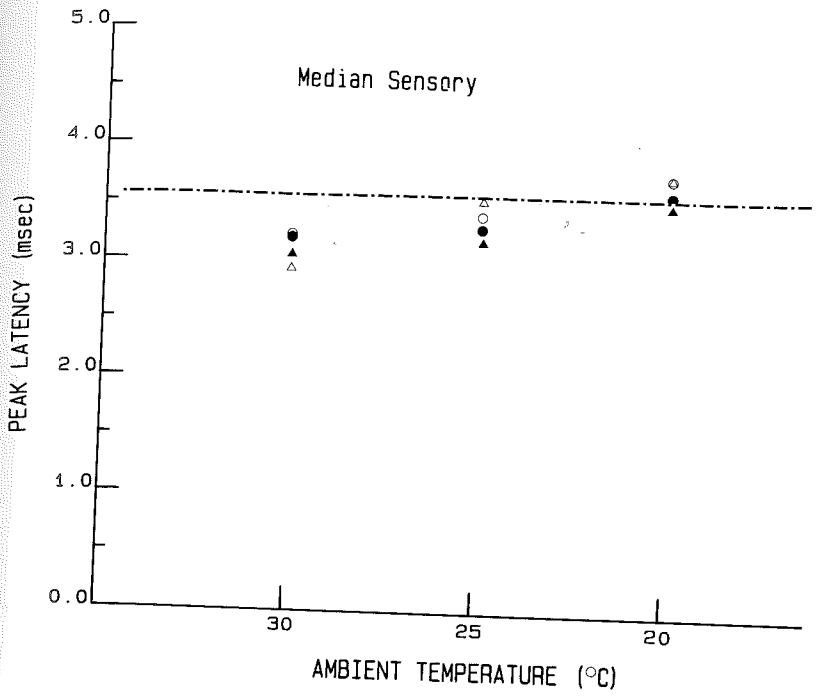

FIG. 4. Median sensory nerve peak latency at each ambient temperature. Dashed line marks upper limit of normal range (3.6 msec).

sensitive to electrical stimuli (slopes 35%-48% greater) on the more affected ($F = 6.7$; $p < .022$) and less affected ($F = 7.0$; $p < .020$) sides as compared to the controls (Fig. 6).

Hand Function Testing

All post-polio subjects reported that the hand function tasks required increased effort at lower T_a. This subjective report was associated in general with increased task completion times at lower T_a. However, there were no significant differences in completion times between the two groups because of the very large variance in completion times within the post-polio group at all temperatures. To control for this variance and to take advantage of the control imposed by the temperature exposure sequence,

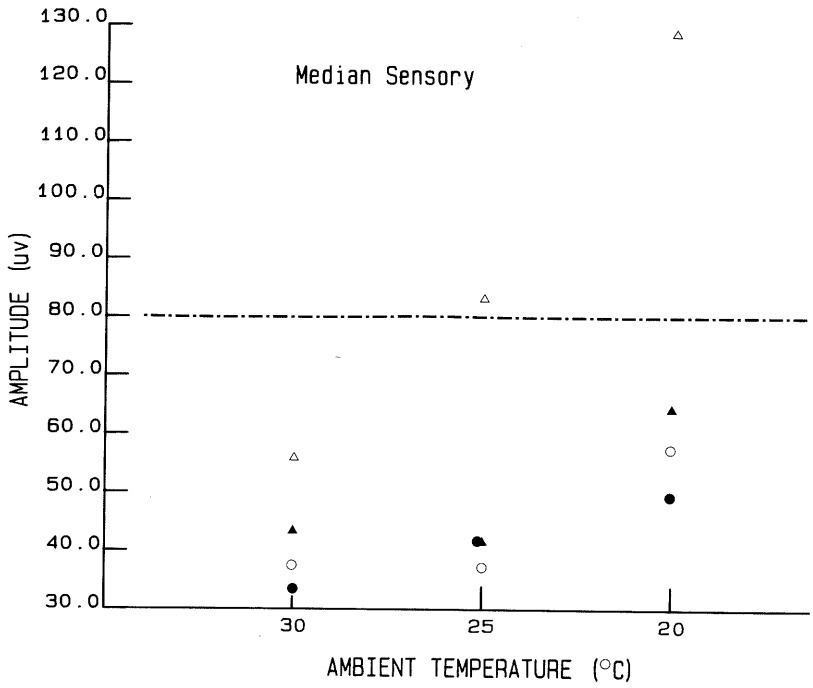

FIG. 5. Median sensory nerve potential amplitude at each ambient temperature. Dashed line denotes 80uV criterion for defining "giant" sensory nerve potentials.

the percentage change in task completion time with increasing T_a (25° - 30°) was compared to that for decreasing T_a (30° - 20°C). There were no significant differences in the percentage change in performance on any subtest between the hands in either group or between the post-polio subjects and the controls. There was also no significant effect of T_a on the percentage change in performance on any subtest in the controls. However, there were significant decrements in performance (70%) with decreasing T_a in the post-polio subjects on both the small common objects ($F = 11.5$; $p < .009$) and large heavy objects ($F = 11.0$; $p < .012$) subtests.

The subjective reports of increased effort and the performance decrements on two of the subtests with low T_a were associated with qualitative changes in motor performance.

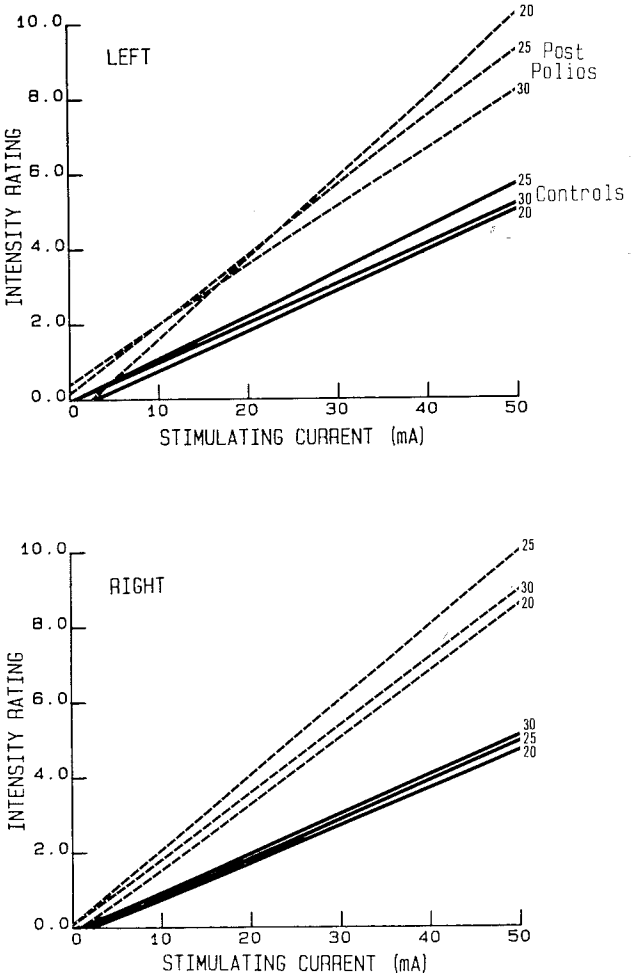

FIG. 6. Linear regression of subjective intensity rating on applied electrical stimulating current at three ambient temperatures as a measure of cutaneous sensitivity.

Prehensile patterns changed from precision grips to power, tenodesis or other facilitory grips at low T_a. In addition, overflow of muscle recruitment to other areas of the body was evident.

Discussion

The finding that post-polio subjects and controls had equivalent decreases in blood flow with cooling suggests that reflex sympathetic vasoconstrictor outflow was normal, and not hyperactive, in these post-polio subjects. The blunted or paradoxical vasomotor response to mental arithmetic in the post-polio subjects suggests that the sympathetic vasoconstrictor response to stress was actually decreased, possibly as a result of damaged pre- and post-ganglionic sympathetic neurons.

The finding of lower mean blood flow at 30 °C in post-polio subjects is probably also the result of damaged sympathetic vasoconstrictor neurons allowing passive dilatation of cutaneous venous capacitance beds. Such dilatation would produce the venous congestion evident in post-polio patients and is associated with decreased arterial inflow to the skin.[9] Cutaneous venous pooling combined with a decrease in warm blood flowing to subcutaneous tissues will promote thorough and efficient heat loss and produce the markedly cold limbs seen in post-polio patients.[14,15]

It is this deep and thorough limb cooling that accounts for the recording of clinically abnormal nerve latencies in the post-polio subjects at skin temperatures equal to those of the controls. At equivalent skin temperatures, both subcutaneous tissue and nerve temperatures will be lower in the post-polio patients, and nerve latency will be prolonged beyond that which would be predicted by skin temperature in the controls. The reported resistance of already cold limbs to warming is also related to thorough limb cooling. As tissue temperature drops, the sensitivity of vascular $alpha_1$-adrenoceptors (the receptors that cause vasoconstriction in response to norepinephrine release) increases.[16] This increase in receptor sensitivity accentuates vasoconstriction, further reducing the flow of warm blood to the skin, and tissue temperature continues to plummet. This cycle of cooling through radiant heat loss, increasd adrenoceptor sensitivity, decreased blood flow and further tissue cooling may serve to maintain low limb temperature.

The finding of bilateral hypersensitivity to electrical stimuli in the post-polio subjects was unexpected and must be replicated. The occurrence of the "giant" sensory nerve potentials in the post-polio subjects corroborates the findings of Ginzburg et al[17,18] but does not seem to be related to the hypersensitivity,

since giant sensory amplitudes were prominent on the more affected side and increased with decreasing temperature, while the hypersensitivity was equal bilaterally and was not augmented by temperature. The mechanism of cold-induced pain has yet to be described in post-polio patients or in controls, although it is clearly related to vasoconstriction.[19] The cold-related pain and hyperesthesia in post-polio patients' affected limbs may be caused by the effects of profound vasoconstriction and cooling being heightened by a generalized hypersensitivity to pain.

This study is unable to describe the mechanism responsible for the post-polio subjects' impaired manual dexterity and for the increased effort required to perform motor tasks at low T_a. Increased motor nerve latency at low T_a (i.e., decreased nerve conduction velocity) associated with a prolonged muscle refractory period and lengthened motor action potential has been implicated in cold-induced decreases in muscle performance because they may "limit the number of efferent stimuli reaching the muscle."[20] Further investigation is required to document the pathophysiology of the cold-induced impairments of normal and reinnervated muscle functioning.

Acknowledgments

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Late Effects of Poliomyelitis: Clinical Pathophysiology

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Introduction

Over the past five years, an increasing number of persons who contracted poliomyelitis during the major epidemics of the 1950s and the 1960s have reported changes in muscle function. These changes are characterized mainly by weakness and fatigue which have developed about 25-30 years after the initial onset of poliomyelitis and have involved mainly the muscles that had previously been weakened during the initial onset but which had recovered sufficiently to provide the individual with appropriate function in activities of daily living and work-related activities.

The great majority of individuals give a history of having witnessed this general decline in muscle function, which usually began about five years prior to being seen, and which resulted in severe dysfunction requiring the need of an increased use of ambulation aids and frequently a change from bipedal ambulation to the use of a wheelchair. These people appear to have an awareness of their body sufficient to clearly identify the muscle groups that have become weaker and have the ability to describe what has happened to their musculoskeletal system in a way which is much more exact than the average population. Their history indicates clearly the degree of dysfunction that took place immediately after the initial onset of poliomyelitis and, equally clearly, the recovery pattern that occurred and more recent decline patterns in this system. Characteristically, the description is one

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of initial weakness either of a paraplegic or quadriplegic or sometimes hemiplegic type, with the more rare incidence of localized muscle weakness, followed by improvement in function of some of the muscles which had become weak during the initial onset. After a period of 25-30 years, this is followed by a decline in function of many, if not all, of the muscles that had improved in function following the initial onset and weakness. It is this most recent decline that results in severe dysfunction involving many aspects of activities which these individuals had been able to do previously without difficulty.

Attempts at getting medical help for this recent decline have most frequently been met by the idea that after 20 years of good function, there is probably nothing which can be done to improve these patients and with this idea presented to them repeatedly, they have accepted the decline and the accompanying dysfunction and need for more intensive use of ambulation aids, other help, or wheelchairs.

In this study, these patients have been evaluated by electrophysiological studies and consistent changes have been noted in EMG as well as on repetitive stimulation studies. With the increasing number of patients demonstrating very similar electrical activity in these muscles that have recently experienced a decline in function, the electrophysiological studies have been helpful in identifying the groups of muscles that are amenable to strengthening exercises in physiotherapy. This very specific approach toward physiotherapy, combined with teaching methods to improve function by occupational therapy and modification of bracing and more appropriate orthotic management, taking advantage of the most recent advances in this latter area, has resulted in improvement in function and the reversal of the pattern which had been developing over a period of at least five years.

The multidisciplinary approach toward the management of the late effects of poliomyelitis has been attempted on an outpatient as well as an inpatient hospital basis. This choice is dependent primarily upon the severity of the decline and on whether the patient lived close to the multidisciplinary facility, relating this to whether the patient would tire easily as a result of the need for transportation to and from the outpatient facility.

Methods

The University of Alberta Hospitals in Edmonton, Alberta, was one of the hospitals which received a very large number of patients soon after their onset of poliomyelitis during the major epidemics. Acute care as well as follow-up care of these patients was undertaken by the hospital and good records have been kept regarding follow-up of these patients. Most recently, there has been increasing interest in the respiratory changes that have taken place in these individuals over the last 20 years, and many of them have been seen in review by the respiratory service. With the increasing complaints of musculoskeletal changes, a seminar was held in November 1983, to which were invited all the patients on whom follow-up had been continued because of the need for medical care resulting from the initial onset of poliomyelitis and ongoing complications. Seventy patients came to the seminar. Many of them continued to have respiratory difficulties and an almost equal number had musculoskeletal changes which had become more accentuated over the past five years. The seminar dealt with the medical management of respiratory problems, a review of some difficulties resulting in late musculoskeletal changes in poliomyelitis patients, as well as presentations from orthopedic specialists on the various aspects of treatment of scoliosis in poliomyelitis patients. In addition, there was paramedical input regarding social service and community resources available to the disabled population of Alberta.

Following a very preliminary report to them on what appeared to be a trend developing with individuals in their group regarding the development of muscle weakness and fatigue, a large number of patients came forth indicating that they had noted changes in muscle function similar to those described in the seminar. We were impressed by the way in which they were clearly able to identify these muscle groups and equally impressed by the way in which they had attempted to get help when they observed these changes and were told that nothing was medically known that could be done for them.

Arrangements were made for these individuals to be evaluated clinically as well as with electrophysiological studies,

and the first 12 patients in this group formed the basis for this initial report.

On their first visit, the patients presented a history which indicated repeatedly that they had, in fact, had poliomyelitis during the epidemics, had identified areas of severe weakness as a result of the initial onset, had witnessed improvement in function in keeping with the degree of recovery of some muscle groups and had, more recently, noted returning weakness mostly in these muscles that had previously recovered from the initial involvement with the disease.

Physical examination was geared toward identification of any musculoskeletal abnormalities that could be found and, indeed, severe weakness frequently demonstrating less than antigravity strength in some muscle groups was encountered.

With the appearance of these changes in muscle function, patients were subjected to electrophysiological studies. These included motor nerve conduction velocity studies of the nerves leading to the muscles that have been identified clinically as being weakened, EMG studies of normal as well as weakened muscles and repetitive stimulation studies of the neuromuscular junctions or normal functioning nerves and muscles, as well as those that had been identified in the group where recent weakness had taken place.

Following this initial evaluation, the patients were divided into two groups, depending upon the severity of dysfunction and whether they lived a long distance away from the hospital or whether they could easily come in as outpatients on a daily basis. Of the total of 12 patients who were studied initially, 6 were admitted as inpatients, 6 were seen as outpatients, including one who required only a change in bracing without any other changes.

When patients were seen in the treatment areas of physiotherapy and occupational therapy, they were evaluated from a point of view of muscle function, ambulation and transfer ability. They were then evaluated further on a functional mobility scale which had previously been developed for other individuals with neuromuscular or musculoskeletal disability. If they were to enter into the treatment program as inpatients, they were admitted into the hospital prior to the initial treatment area evaluation and were followed up by treatment as inpatients. Reevaluation was done at least twice during their inpatient stay. If they

were to continue as outpatients, they were evaluated just prior to the start of outpatient therapy and were reevaluated again at the same intervals as inpatients and again upon discharge from the program.

The method of treatment, whether inpatient or outpatient, consisted of strengthening progressive resistive exercises, sometimes beginning by elimination of gravity and maintaining range of motion, followed by repetitions against gravity depending on the patient's tolerance. As function of the muscle groups that had been weakened improved, weights were added against which the patient did the exercise. In this way strengthening took place over time. We were always aware of the danger of overexercise resulting in debilitating fatigue which seems to be a characteristic of these muscle groups. For this reason, it was emphasized to the therapy staff that progress be slow but steady in attempting to strengthen the weakened muscle groups. One patient had previously been overexercised and had noted this adverse reaction. Once the patient had achieved 20 repetitions, either against gravity or against a weight as resistance, the weight amount was increased and the patient began exercising with five repetitions at each attempt gradually increasing up to 20 repetitions as tolerated.

These patients presented frequently with orthotic devices which had been prescribed for them at the time that they had their initial poliomyelitis with rare, if any, reevaluation since. Therefore, with the use of polypropylene and similar materials, not only in short-leg ankle-foot orthoses (AFO) but also long-leg knee-ankle-foot orthoses (KAFO), the latter with the use of metal knee joints, we had the opportunity of substantially lightening the weight of the braces that were being used, and we took advantage of this in prescription of new braces. In addition, where it was possible, for example, to strengthen quadriceps muscles to the point where they were at least antigravity in strength, we were able to reduce the size of the brace frequently from a KAFO to polypropylene AFO to provide proper heel strike and toe elevation during the gait cycle, thereby changing entirely the method of walking and improving the efficiency and quality of gait.

The use of lighter weight bracing permitted us to encourage patients to do more walking over longer distances and use the wheelchair less, and we were successful in starting bipedal am-

bulation in patients who had previously presented in wheelchairs.

The length of time the patients were treated as inpatients varied from five to eight weeks and, when possible, the patients were allowed weekend passes. The length of time that was needed for outpatient treatment was up to 12 weeks at a treatment frequency of anywhere from three to five times weekly.

Follow-up demonstrated maintenance of gains that were obtained while under treatment. At the present time, there is a continuing influx of patients fitting the description already mentioned who are being subjected to evaluation and treatment according to the protocol presented here.

Results

On initial evaluation of these patients, whose ages ranged from 33 to 74, we were able to identify the reasons for deterioration in muscle function. The muscles that had been identified as being weakened demonstrated muscle strength of anywhere from grade 2/5 to grade 4/5 and there was a correspondence between the complaints of weakness and the decrease in muscle strength seen on examination. (This is on a grading system of 1 to 5 in which grade 1 represents a barely palpable muscle contraction, grade 3 represents the ability of the individual to perform one joint range of motion against gravity and grade 5 represents unbreakable muscle contraction.)

Electrophysiological changes in these muscles demonstrated absence or virtual absence of insertional activity. Despite this, attempts at voluntary movement of the same muscle without needle movement demonstrated normal-appearing motor unit potentials (mup) with normal amplitude and duration being noted in these mup's. There was generally a reduction in the interference pattern to as low as 20% to 25% of normal, but we saw only rarely the presence of polyphasic potentials or fasciculations in these muscles, so that we felt that the abnormalities seen on EMG were not due to anterior horn cell disease. In addition, repetitive stimulation studies demonstrated usually a decrement, unaffected by exercise, as low as -25. However, we occasionally also saw increments of up to +10 and sometimes noted a decrement followed by an increment in the same muscle. Tensilon test was not done.

Patient response to strengthening exercises in physiotherapy is demonstrated in Tables 1-3. Gains of as much as two grades were noted during the treatment process, both for inpatients as well as outpatients. Besides definite increase in strength, the significance of this improvement was that we were then able to improve function of these patients, permitting more appropriate ambulation as well as the opportunity of changes in orthotic management. For example, in the case of J.L. (Table 1), the presence of improvement to grade 5 in the right knee extensors and grade 4+ in the left knee extensors permitted her once again

Table 1. Muscle Testing - Mrs. J.L. - Outpatient

	Initial Assessment *Dec. 7/83*	*Feb. 22/84*	*Mar. 21/84*	*Apr. 12/84*
Right-knee extensors	3	4	4+	5
-hip flexors	3+	4	4+	5
-hip abductors	4	4+	4+	5
Left-knee extensors	3	3+	4+	4+
-hip flexors	3+	4	4+	5
-hip abductors	4	4	5	5
Abdominal musculature	3+	4	4	5

to be able to come to a standing position from a sitting position in a chair. To her, the return of this skill was of great importance. The improvement in abdominal musculature strength from grade 3+ to grade 5 contributed to this as well. Initially, she was falling daily but after treatment, her frequency of falls reduced to zero, thereby eliminating the possibility of injury.

The results obtained on patient G.G. (Table 2) permitted us to change his left KAFO to a left AFO with his knee extensors and knee flexors being strong enough to control his knee with the help of a polypropylene AFO. Similarly, improvement in right shoulder and knee function permitted the patient to use his arms better and reduce his pain complaints in his right upper limb and right knee by providing better support for these areas. An additional benefit was that he was able to walk for much longer distances than he had previously.

Table 2. Muscle Testing - Mr. G.G. - Outpatient

	Initial Assessment			
	Aug. 24/83	*Jan. 13/84*	*Feb. 29/84*	*Apr. 12/84*
Left-hip abductors	3	3+	4	5
-hip flexors	4	4	4+	5
-hip extensors	4	4	4+	5
-knee extensors	2	2	3	3+
-knee flexors	3	3+	4	4+
Right-shoulder abduction	3	3	3+	4+
-shoulder flexion	3+	4	4	4
-elbow flexion	4	4	4	5
-elbow extension	4	4	4	4+
Right hand grasp	3+	3+	4	5

Mrs. J. McL. (Table 3) was unable to transfer out of her wheelchair when first seen. Despite respiratory compromise, she progressed with inpatient treatment to where she was able to walk 50 feet with a walker without the use of oxygen and 250 feet with portable oxygen use. She had been totally dependent upon continuous oxygen prior to starting the program. Her improvement permitted her much more active involvement in home and community activities and she was able to take a volunteer position at the University Hospital. In addition, after initially being known as "the case of the disappearing whistle," she was able to again whistle tunes quite happily with improvement in abdominal muscle strength.

Discussion

The results of this study permit us to identify more exactly some of the changes that take place in muscle groups of individuals who have previously been afflicted by poliomyelitis and who have recovered, with particular emphasis on secondary late changes in the muscle groups that had recovered. These changes have been manifested clinically by weakness resulting in a decrease in function in areas in which these muscle groups are required, together with generalized fatigue. A possible explanation for the pain that is frequently experienced by these patients is offered. Lack of support of underlying joints resulting from muscle weakness is suggested as one possible cause of pain.

Electrophysiological studies demonstrate changes which are

Table 3. Muscle Testing - Mrs. J. McL. - Inpatient

Hospital Admission	*Oct. 3/83*	*Oct. 21/83*	*Oct. 26/83*	*Discharge Nov. 10/83*
Left-hip abduction	3	4	4	4
-hip flexion	4	4	4	4
-hip extension	4	4	4	4
-knee flexors	3	4	4	4
-knee extensors	2+	2+	3	3
-ankle dorsiflexion	3	3	3	3
-toe extension	3	3	3	3
Abdominals	2	2	3	3
Ambulation (WC only)				
- without O2		30′	40′	50′
- with O2		80′	100′	250′

really quite specific for this clinical entity and are unlike any other electrophysiological changes seen in other neurological or musculoskeletal clinical entities. The exact reason for these changes remains obscure.

The use of a specific goal-oriented multidisciplinary approach involving inpatient or outpatient physiotherapy and occupational therapy and orthotics permits us to improve the strength of the muscle groups that have become weakened and thereby improve function of these patients. In addition, the improvement of muscle function permits us to take a critical look at previous orthotic management and to make appropriate changes to reduce energy consumption in ambulation and, therefore, ambulation tolerance. The changes that take place in muscles as a result of this approach are presently unknown and will certainly require additional closer study. This multidisciplinary approach permits us to identify muscles that need treatment and permits patients to benefit from a specific and logical effort at improvement of function with reduction in energy consumption in performing these functions.

Epidemiology

Poliomyelitis in Rochester, Minnesota, 1935-1955: Epidemiology and Long-Term Sequelae: A Preliminary Report

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Introduction

The onset of muscular weakness and atrophy many years after an acute episode of paralytic poliomyelitis has been reported numerous times in the past 100 years.[1-11] Recent interest in this "syndrome" has stemmed from the fact that among the many thousands affected by polio in the epidemic years of the 1940s and 1950s, some are now experiencing new difficulties which have been ascribed to their old polio. Patients with "post-polio syndrome" described in the earlier studies were drawn largely from referral practices and, thus, reflect a selection bias, both in numerical terms and in terms of disease severity. More recent studies have also concentrated primarily on cases of post-polio syndrome. Thus we have to date no accurate information regarding the proportionate frequency of this syndrome relative to the total cohort of paralytic poliomyelitis victims.

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In an effort to address this issue, we have conducted a study of poliomyelitis in the population of Rochester, Minnesota. In this preliminary communication, we will (1) describe some of the epidemiologic features of poliomyelitis in Rochester from 1935 through 1955 and (2) discuss follow-up data on the cohort of patients with a diagnosis of paralytic poliomyelitis during those years.

Epidemiology

Patients and Methods

The centralized records-linkage system at the Mayo Clinic provides a unique opportunity to conduct population-based research.[12] Residents of Rochester and surrounding Olmsted County have for many decades received their medical care primarily at Mayo Clinic and its affiliated hospitals. Diagnoses have been indexed since 1907 and processed for automated retrieval since 1935. Diagnoses of Olmsted County residents receiving medical care at other institutions in Rochester and surrounding counties are similarly coded and processed, thus insuring virtually complete ascertainment of major illnesses for this delineated population.

For the purposes of this study, histories were retrieved using all diagnostic codes pertaining to spinal and/or bulbar poliomyelitis including infantile paralysis, cerebral paralysis and bulbar paralysis. Patients were required to have had established residence in Rochester prior to diagnosis for inclusion in the study. All case reports were reviewed and classified to the diagnostic groups defined below.

Diagnostic Groups

Polio "suspects." This term was used by the physicians in the polio epidemic years to describe persons with an acute febrile illness suspiciously similar to polio but without paresis or evidence of central nervous system involvement from clinical history and/or cerebrospinal fluid examination. Many of these persons were family members and contacts of cases. Some may have had abortive polio and may constitute the "tip of the iceberg," since so many cases of polio never came to the attention of the physi-

cian. This group is important, however, because of its contribution to the transmission of disease and its part in individual and herd immunity.

Nonparalytic poliomyelitis. Cases of nonparalytic polio were defined as those with an acute febrile illness, constitutional symptoms suggestive of CNS involvement (i.e., headache, neck rigidity and signs of meningeal irritation) confirmed by the finding of pleocytosis and increased protein in CSF. Some authors include in this group patients with initial and transient paralysis. We have chosen to include 12 patients who had questionable weakness or transient, mild paresis of less than 72 hours duration.

Paralytic poliomyelitis. A history of an acute febrile illness with positive findings on CSF examination and the existence of weakness or paralysis was taken to be diagnostic of paralytic poliomyelitis. However, 25 patients in this group did not have a CSF examination at the time of the febrile illness. All had paralytic residua of the illness and many were contacts of patients diagnosed and treated for poliomyelitis at Mayo Clinic.

Results

Incidence. Between 1935 and 1955 there were 131 patients with sufficient clinical information to be classified as polio "suspects." There were 316 patients with a diagnosis of poliomyelitis in the same period. Of the 316, 201 had paralytic polio and 115 had nonparalytic polio. Figures 1 and 2 show the distribution by year of onset of paralytic cases and nonparalytic cases, respectively. Just over 50% of all cases occurred in 1952. Figure 3 compares rates per 100,000 population for Rochester and the rates for the United States. The average annual incidence rate per 100,000 population for Rochester was 56.1. The rate for 1952 alone was 470 per 100,000.

Sex. The overall male to female ratio was 1.08:1.0. However, females were slightly more commonly affected by paralytic polio (M/F = 0.92) and males by nonparalytic polio (M/F = 1.27).

Age. The average annual age-specific rates for paralytic and nonparalytic polio are given in Table 1 and Figure 4. Both forms of polio occurred most commonly in the 0-9 age group with a secondary rise in the 25-34 age group. The age range was 0 to 59 years with a median age of nine years.

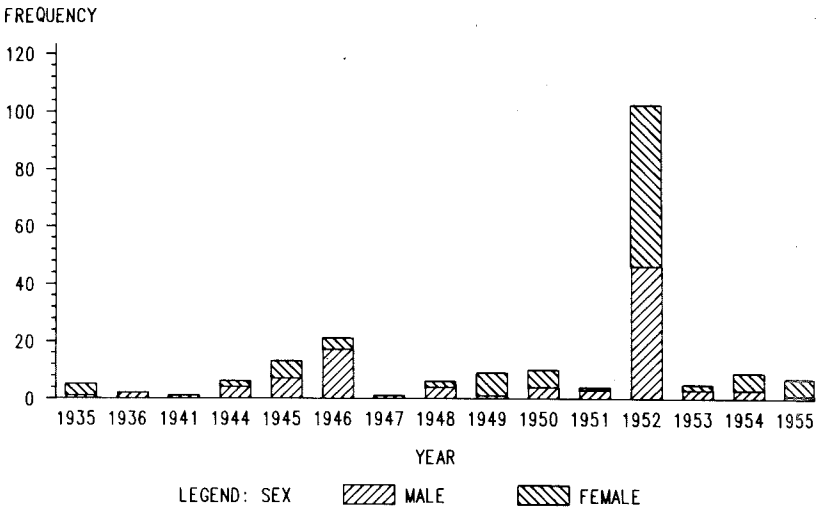

FIG. 1. Paralytic polio: cases by year of onset.

Average annual age- and sex-specific rates for polio indicate that in the 0-9 age group, males were more commonly affected while in the 25-34 age group, females were more commonly affected (Table 2 and Figure 5).

Seasonal pattern. Figure 6 shows the seasonal pattern of occurrence of poliomyelitis, all years combined. Cases occurred from May to December with peak occurrence in September (approximately 30% of all cases). Twenty-seven percent occurred in August, 21% in October and 18% in July.

Familial aggregation. While there was evidence of familial aggregation of poliomyelitis cases, it was impossible to define clearly the exact pattern. This is mainly because we cannot construct denominator information in terms of household members. We hope to provide more detailed information in the completed report.

Poliomyelitis: Symptoms at Onset

The mean duration of symptoms prior to diagnosis was 4.5 days. Day of diagnosis was defined as the day of examination

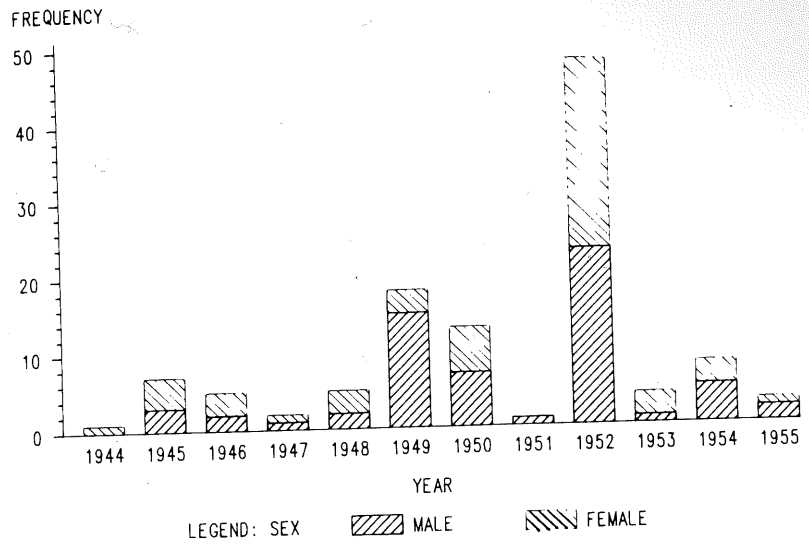

FIG. 2. Nonparalytic polio: cases by year of onset.

of CSF which in the vast majority of cases was the day of presentation to a physician.

Twenty-five percent of patients exhibited a biphasic prodrome, i.e., an acute febrile illness lasting two to three days followed by remission and subsequent development of a second febrile illness with or without paralysis. Fever, stiff neck and anorexia were the most common presenting features, each occurring in more than 95% of patients. Headache and malaise were present in two thirds and gastrointestinal disturbances in one third. Muscle stiffness, in particular of lower limb musculature, and back stiffness was a common presenting symptom in the absence of paralysis.

Paralysis in the Acute Phase (201 Cases)

Ninety-four percent of patients had spinal paralysis either alone (approximately 60%) or in combination with bulbar or respiratory paralysis. Bulbar paralysis, i.e., involvement of upper and lower cranial nerves, occurred in 38% of patients.

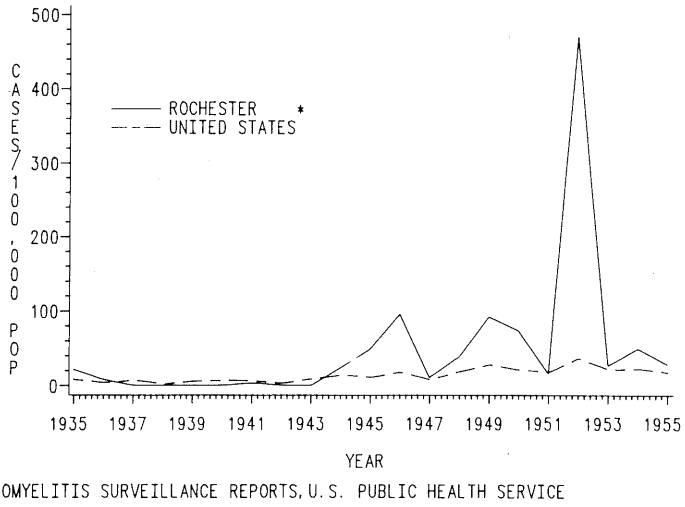

FIG. 3. Annual poliomyelitis incidence rates.

Respiratory paralysis occurred in 16%. Clearly, there is overlap between the different sites of involvement. However, because a high proportion of those with bulbar or respiratory involvement succumbed in the acute phase of the illness and because our follow-up group is composed primarily of those with spinal involvement, we have confined our present discussion to this latter group. Thus, the estimate of the relative frequency of post-polio syndrome which we have derived is defined with respect to the cohort of patients with spinal involvement.

In defining spinal paralysis according to severity, a scale of 0 (zero) to -4 (minus four) is used, where 0 is normal and -4 implies complete paralysis. Three categories of severity are arbitrarily defined as follows: 0 to "-1" involvement of one or two limbs constitutes mild paresis; 0 to "-1" involvement of more than two limbs or "-2" to "-3" involvement of one or two limbs constitutes moderate paresis; "-2" and "-3" involvement of more than two limbs or "-4" (paralysis) in any limb constitutes severe paralysis (Table 3). Among our patients with spinal paralysis, 33% had mild involvement, 40% had moderate involvement and 27% had severe involvement.

Case Fatality Ratio

Of 201 patients with paralytic poliomyelitis, 23 died in the acute phase of the illness, a case fatality ratio of 11.4%. The age range was under 1 year to 59 years with median age of 17 years. The age range of this group is identical to that of the total cohort of polio patients. The median age of this group, however, is considerably higher, being almost double that seen in the total cohort (9 years). There were 13 males and 10 females. Twenty-six per-

Table 1. Average Annual Age-Specific Rates of Poliomyelitis per 100,000 Population: Paralytic vs Nonparalytic Poliomyelitis in Rochester, Minnesota

Age	*Paralytic (N = 201)*	*Nonparalytic (N = 115)*	*Total (N = 316)*
0 - 4	109	58	167
5 - 9	112	68	180
10 - 14	44	44	89
15 - 19	34	11	45
20 - 24	25	11	35
25 - 29	41	20	62
30 - 34	46	25	70
35 - 39	13	2	15
>40	3	2	5
Total	36.0	20.1	56.1

cent had bulbar paralysis, 22% had respiratory paralysis and 52% had both bulbar and respiratory involvement.

Figure 7 shows deaths by year. The seven deaths in 1945 constitute 33% of all cases diagnosed in that year, whereas the ten deaths in 1952 represent 10% of cases diagnosed in that year. The decrease in case fatality rate from 1945 to 1952 may be due to improved respiratory equipment, different viral type or a combination of both.

Deaths in Interim Years

There were seven deaths in subsequent years. In four, all of whom had minimal residua of polio, deaths were from causes apparently unrelated to polio. There were two males, both of

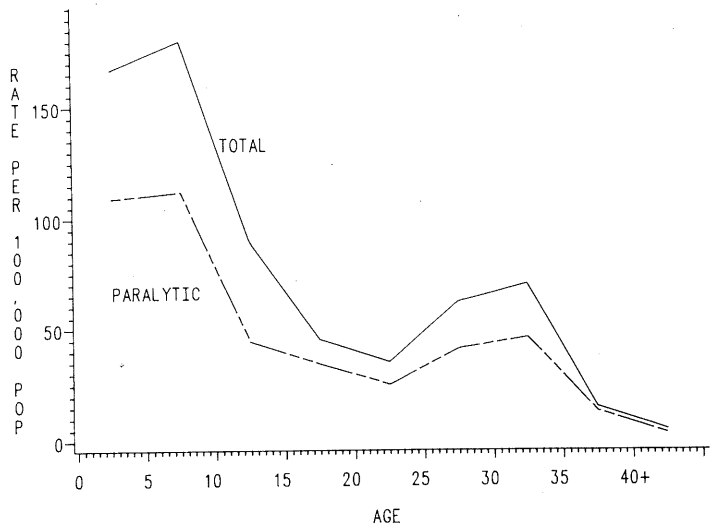

FIG. 4. Average annual age-specific rates for poliomyelitis (per 100,000 population: paralytic vs total).

whom committed suicide 10 and 12 years, respectively, after the onset of polio. There were two females who succumbed to other illnesses 46 and 47 years, respectively, after the onset of polio. In contrast, three people with severe involvement with polio during the 1952 epidemic died later from complications of the illness. There were two females and one male. All were quadriplegic with respiratory paralysis. All had residual respiratory insufficiency and died from respiratory complications. One of the three patients had severe recurrent urolithiasis, with renal osteodystrophy and hypertension.

Follow-Up

Patients and Methods

For follow-up, a questionnaire was circulated in April 1984 to all traceable patients who had had paralytic poliomyelitis. This inquired about general health status. Specific inquiries regarding muscular weakness resulting from polio were made. Subjects were

asked to indicate the time required to achieve their maximal functional recovery following polio, whether the residual weakness had remained static or worsened since their maximal recovery and if worsened, how long since they had first noticed this change. Patients were asked to indicate other problems resulting from polio and any medical or surgical interventions since their last contact with the Mayo Clinic.

This questionnaire was supplemented by a detailed telephone interview for those who indicated deterioration since their maximal functional recovery from polio. In this interview, the subjects

Table 2. Average Annual Age-Specific Rates of Poliomyelitis per 100,000 Population: Male vs Female Poliomyelitis in Rochester, Minnesota

Age	*Male*	*Female*	*Total*
0 - 4	178	156	167
5 - 9	221	139	180
10 - 14	94	84	89
15 - 19	53	41	45
20 - 24	22	39	34
25 - 29	44	71	60
30 - 34	67	73	70
35 - 39	28	5	15
>40	6	4	5
Range	0 - 59	0 - 48	0 - 59
Median	6	13	9

were questioned about excessive fatigue, decreased endurance, extent of muscle weakness, fasciculations, muscle cramps, muscle and joint pain, atrophy, contractions and deformity. Activities of daily living and increased needs for walking aids, wheelchair, personal and ventilatory assistance were discussed. In addition, patients were asked about intercurrent illness, surgical procedures, falls and fractures.

Results

Of 171 potential respondents being followed from 30 to 50 years after their acute polio, 23 remain untraced at the time of presentation of these data. Some of these may still be traceable.

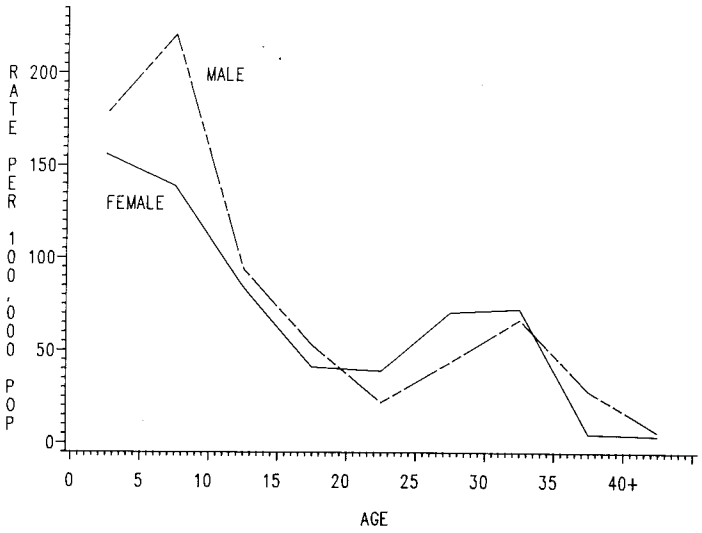

FIG. 5. Average annual age-specific rates for poliomyelitis - paralytic and non-paralytic (per 100,000 population: male vs female).

Replies have been received from 128 of the remaining 148 patients or a response rate of 86%. Of the 128 respondents, three persons were unwilling to participate. Of the 125 remaining, 97 patients indicated stability and 28 indicated deterioration since their maximal recovery from polio. This represents a rate for deterioration since maximal recovery among paralytic poliomyelitis victims of 22.4%. This is based on participating respondents. The medical records of those nonresponders to date and those untraced to date have been examined for evidence of nonparticipant bias. There was no evidence that the proportions of patients in the mild, moderate and severe categories previously described were different among nonparticipants. Thus, we assume that participants and nonparticipants had the same spectrum of initial involvement with poliomyelitis.

The specific complaints among this group of 28 patients who indicated deterioration since their maximal functional recovery from polio are as shown in Table 4. None of these patients reported signs or symptoms of classic amyotrophic lateral

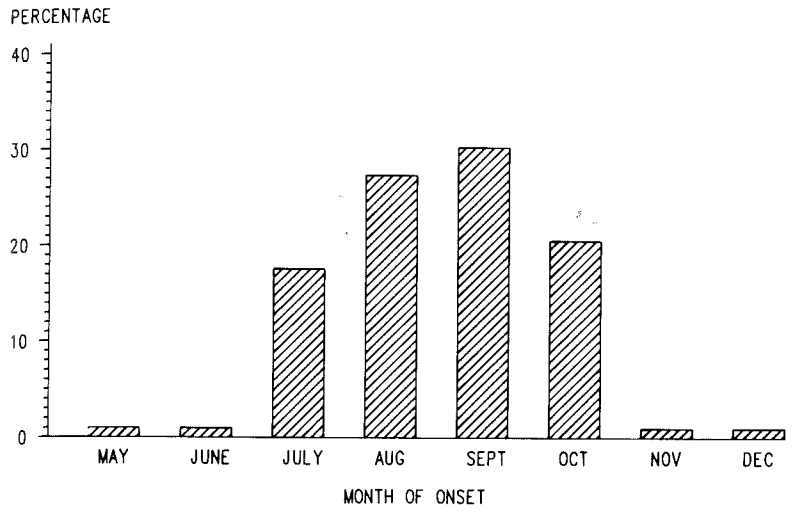

FIG. 6. Seasonal variation of poliomyelitis.

sclerosis. The interval between the initial attack of poliomyelitis and the onset of new problems ranged from 12 to 35 years with a median of 25 years.

Summary

One hundred twenty-five patients who had paralytic poliomyelitis in the period between 1935 and 1955 have been followed from 30 to 50 years. Ninety-seven of these patients have no new symptoms related to their poliomyelitis. Twenty-eight patients report that they have had progressive symptoms related to their previous episode of acute poliomyelitis. We are presently undertaking a study to determine the nature of these new symptoms. Our preliminary observations suggest that in some patients the new symptoms are related to aging, in others to new illness (i.e., malignancy) and, in others, to drug abuse (alcoholism). It is apparent, however, even in this initial review that there are patients included in this study who have had recent muscle wasting and weakness which seem clearly related to their previous poliomyelitis. Such variables as age at onset of poliomyelitis, extent

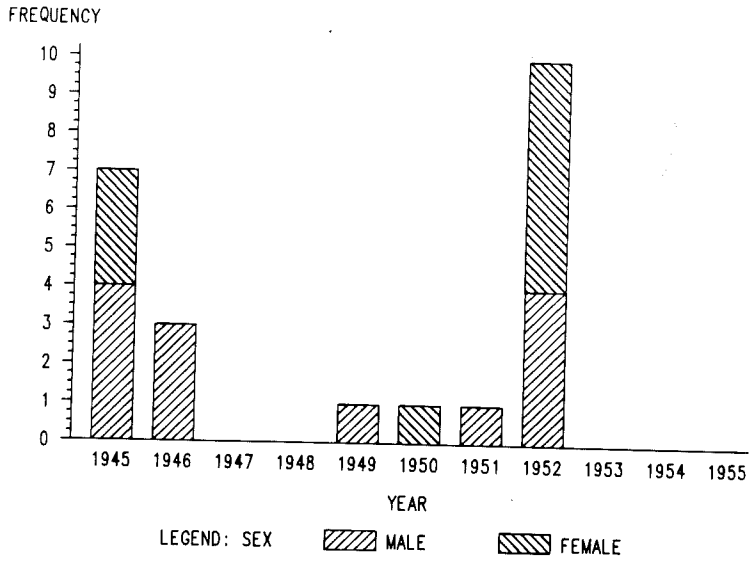

FIG. 7. Death in the acute phase of disease by year.

and severity of paralysis, time to achieve maximal recovery and age at follow-up of these patients will be addressed in the completed report on the possible associations between poliomyelitis and deterioration in later years.

We are impressed that the vast majority of patients demonstrate a continuing ability to successfully adapt despite severe poliomyelitis sequelae.

Table 3. Spinal Paralysis - Severity* Poliomyelitis in Rochester, Minnesota

Mild (≥ "-1" and 1 or 2 limbs involved)	33%
Moderate (≥ "-1" and >2 limbs involved) ("-2" to "-3" and 1 or 2 limbs involved)	40%
Severe ("-2" to "-3" and >2 limbs involved) ("-4" in any limb)	27%

*Using a scale of "0" to "-4."

Table 4. Poliomyelitis - Long-Term Sequelae in 28 Patients Poliomyelitis in Rochester, Minnesota

Increased fatigue	59%
Increased sleep requirement	30%
New muscle cramp	51%
New fasciculation	29%
New weakness	71%
• in formerly weak muscles	66%
• in formerly normal muscles	15%
New muscle pain	48%
New joint pain	74%
New muscle atrophy	46%
New or increased deformity	25%
Decreased mobility	25%
Increased need for ambulatory aids	25%
Increased difficulty dressing	14%
Increased need for personal assistance	7%
Change / cessation of occupation	7%

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Epidemiological Issues in Follow-Up Studies of the Impact of Poliomyelitis

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Introduction

This paper is based on a study which took place in the Province of Manitoba, Canada, the purpose of which was to examine the long-term impact of disability among people who developed respiratory or nonrespiratory polio during the epidemics of the 1950s. The findings of this study are reported by Alcock et al.[1,2] There were 3,644 cases of polio registered in the Province between 1950 and 1959. The highest incidence was in 1953, when there were 2,371 cases. Most acute cases and all cases with respiratory involvement were triaged to one central medical facility, the Winnipeg Municipal Hospitals (WMH). This hospital complex was the officially designed treatment center for the Province. The patients admitted to the WMH are the focus of the Manitoba project on the long-term impact of poliomyelitis. The study was developed in two stages; the first stage was restricted to people with respiratory involvement; in the second stage, the study was extended to all those with non-respiratory polio.

The objective is to discuss some of the methodological and conceptual issues involved when researching the long-term consequences of any chronic disability, although the specific reference

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is to polio. The first section will focus on survey design and the difficulties of controlling for selection bias when studies are based on the networks of those who have survived, but who are also the most severely impaired. The second section will look at the problems of measuring functional status among populations of post-polio people. The third section will examine the problems of validating retrospective, self-reported measures of functional status. All three sections will use the design of the Manitoba study to illustrate how these problems may be handled. The final section will present an analysis of data from that study, using it to discuss aging-related changes in functional status.

Section One

Selection Bias and the Historical Prospective Study

The current concern over the relationship between the aging process and the long-term impact of polio has encouraged a spate of new research. The people on whom many of these studies have been based have been contacted through the rehabilitation or polio survivor networks[3] or through the networks of specialized rehabilitation centers.[4] Inevitably, such study populations tend to overrepresent groups with the highest levels of disability, greatest propensity to experience post-polio aging effects and highest current levels of contact with rehabilitation and mutual support programs for disabled people. There are advantages to focusing on individuals with the highest level of need. However, this method of selecting a study population means that those who did not survive are not included in the analysis of the long-term impact of polio. Furthermore, there is a tendency to underrepresent those who recovered so completely that they were no longer counted within the population of the polio-disabled. The omission of either or both these groups limits the ability of any study to generalize from its findings to the experience of the whole generation of people who developed polio. We also need to document the experience of those who did not survive into the 1980s as well as the less disabled for whom the experience of polio is only a vague memory from childhood.

Ideally, three conditions should be met by a study analyzing the long-term effects of any disabling condition and making generalizations applicable to the population at risk: (1) the study

should be longitudinal in design, (2) it should select its sample from as complete a listing as possible of those who developed the condition and (3) it should begin at the point of disease onset. In research on polio and aging, a true prospective design is impossible, but one can use the "historical prospective" design familiar to epidemiologists. For example, rather than starting from a population of patients with lung cancer and inquiring about earlier exposure to asbestos, a "historical prospective" study includes everyone who shared a common exposure to asbestos at some point in their occupational histories. The research objective is to determine how many in this group subsequently developed lung cancer. Such a design provides data on those who did not survive as well as those in whom the asbestos had no apparent effect. Transferring this methodology to research on polio means going back to a list of people as they developed the disease. The aim is to determine what happened to everyone who had polio, including those who did not survive and those who, having completely recovered, had no further contact with specialized services.

Our advantage in the Manitoba study was that we had access to a case register which included all the people with polio who were admitted to the WMH. By using this register as our population frame, we could avoid the selection bias that is inevitable in studies based on contact with a network of polio survivors.

The register listed 1,540 patients who had been admitted and in whom the diagnosis of polio had been confirmed. In the first stage of the Manitoba study, we selected only those who had required mechanical respiratory support; the second stage extended the research to those with nonrespiratory involvement. The sample design for the study is shown in Figure 1; 264 of the patients listed in the register had required respiratory assistance, but those who died within the first 100 days after admittance were excluded from the study, leaving 186 individuals to be traced. In only eight cases was it impossible to determine whether the individual was still alive, although no more than mortality data were available on a few individuals.

Within this group of 186 people, 56 were known to have died prior to March 31, 1980; 24 had died in the hospitals within the first few years and their medical records provided all the infor-

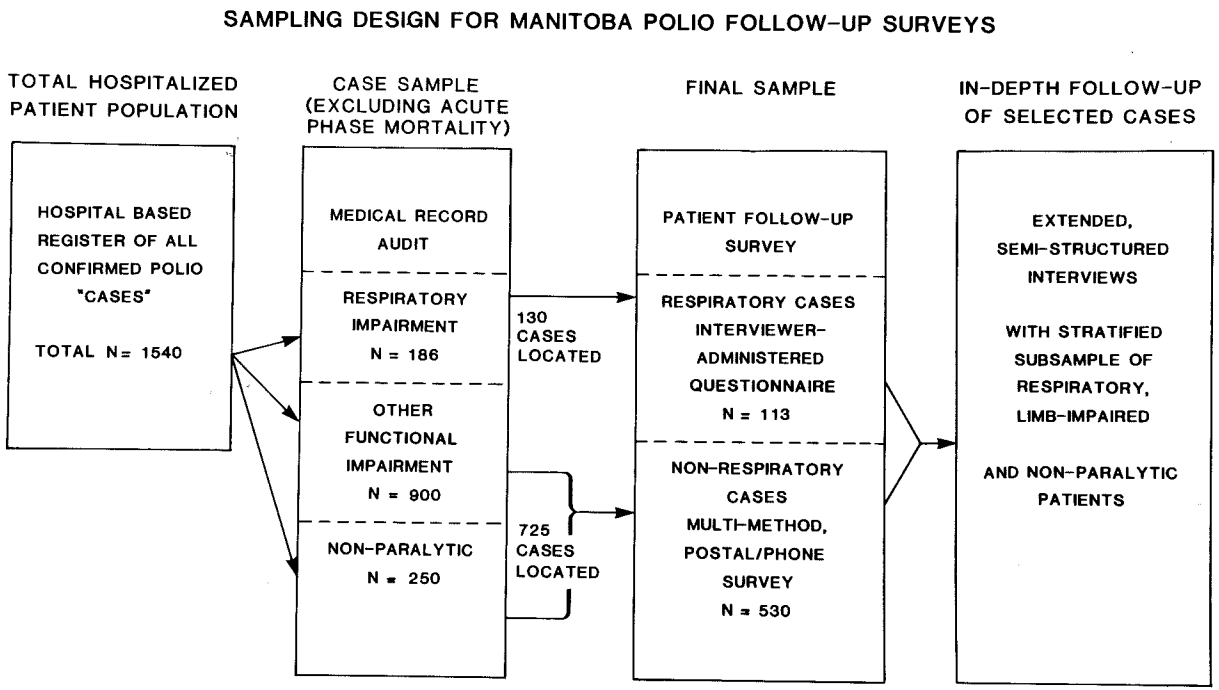
SAMPLING DESIGN FOR MANITOBA POLIO FOLLOW-UP SURVEYS
TOTAL HOSPITALIZED PATIENT POPULATION
CASE SAMPLE (EXCLUDING ACUTE PHASE MORTALITY)
FINAL SAMPLE
IN-DEPTH FOLLOW-UP OF SELECTED CASES
HOSPITAL BASED REGISTER OF ALL CONFIRMED POLIO "CASES"
TOTAL N= 1540
MEDICAL RECORD AUDIT
RESPIRATORY IMPAIRMENT N = 186
OTHER FUNCTIONAL IMPAIRMENT N = 900
NON-PARALYTIC N = 250
130 CASES LOCATED
725 CASES LOCATED
PATIENT FOLLOW-UP SURVEY
RESPIRATORY CASES INTERVIEWER-ADMINISTERED QUESTIONNAIRE N = 113
NON-RESPIRATORY CASES MULTI-METHOD, POSTAL/PHONE SURVEY N = 530
EXTENDED, SEMI-STRUCTURED INTERVIEWS
WITH STRATIFIED SUBSAMPLE OF RESPIRATORY, LIMB-IMPAIRED
AND NON-PARALYTIC PATIENTS

FIGURE 1

mation necessary for the study. Among those who had lived longer and outside the hospital, we did contact and interview the next-of-kin of 26 of the remaining 32 people in the group (in six cases the next-of-kin could not be traced or refused to be interviewed). Of the 130 poeple who were known or thought to be alive, we were able to interview 113. It proved more difficult to trace those with nonrespiratory polio. The register provided sufficient information on only 1,150 patients in this group. We were able to locate and determine what had happened to 725 and questionnaires were sent to and completed by 530.

As you can see from these figures, not everyone we had set out to contact was traced. Inevitably, there are problems of bias. In the first stage we have interview data on 138 out of 186 people, a 74% response rate, but although some next-of-kin interviews were completed, the interview data are biased toward those who survived. Looking only at the representatives of the interview data on the 130 known to be alive, there is bias toward those with the more severe levels of respiratory impairment. (Ninety-seven percent completed questionnaires compared with 76% of those whose medical records indicated minimal effect on the respiratory system.) The reason is that the most impaired were the easiest to find; they were more likely to have remained in Manitoba and to be in touch with the WMH. (This center has remained the main provider of specialist care for respiratory problems associated with polio.)

Despite the difficulties involved in tracing people after such an interval, there are major advantages to the historical prospective design as used in the Manitoba study. We can, for example, document survivorship over the years since the epidemics and can determine which deaths are polio-related. Although the interview data are not representative of the group, we do know where the bias lies. The medical records and the case register allow one to document the age, sex, residential characteristics and levels and types of impairment of all those omitted from the interview process for one reason or another. Any generalizations we would make can be qualified by reference to the representativeness of the group on whom the information is based. It is partly for this reason that the use of the historical prospective design has proved to be important to the Manitoba study. A second reason, however, is that this design has allowed us to deal with one of

the other major problems plaguing research on the long-term impact of disability—the difficulty of establishing a baseline of information on initial impairment levels against which to measure change over time.

Section Two

Measurement of Changes in Functional Ability Among Survivors

The case register provided basic sociodemographic and medical data on each individual. This included age, sex, marital status, type of polio, the use of respiratory equipment, surgical and rehabilitation procedures and levels of impairment both before and after rehabilitation. All these data were recorded as the individual entered the WMH and during the course of their stay in that hospital and are not subject to any recall bias.

Without medical record-based data on people's status during the acute and early rehabilitation phases, most studies of disability have to rely on what individuals can recall about their initial condition. In terms of current research interest in polio and aging, this requires asking people to think back over 20 to 30 years, a problem further complicated by the fact that many were children at the time and have only limited memories of that period in their lives. The design of the Manitoba study provided us with a double opportunity. First, we could use medical records rather than people's memories as a source of information on their functional status at onset; second, we could ask people to recall what their condition had been and then compare what they said with the medical record data. These comparisons are methodologically interesting as a means of validating retrospective data, but they also provide insight into how people retain the memory of traumatic events in their lives.

The medical record data had been recorded according to the needs of the hospital at that time. To be of use in the research context, they needed translating into categories which could also be used when asking individuals to make their own assessment of their past and present condition. To achieve this result, three indices were developed measuring, respectively, respiratory status, mobility, and the ability to carry out the activities of daily living. The format of the indices was designed for use in self-

administered or interviewer-administered questionnaires as well as the protocol for the medical record audit. This audit was separate from the follow-up survey and was carried out by two clinicians who had been members of the medical team involved in the 1952 and 1953 epidemics in Manitoba. Therefore, they were familiar with the records and the manner in which data had been entered at that time.

In view of the diversity of functional assessment systems currently being used in research on post-polio aging, it may be useful to summarize each of the three dimensions of functional ability used in the Manitoba study: respiratory status, mobility and the ability to perform the activities of daily living.

Measures of Respiratory Status

Respiratory status in both the questionnaire and medical record audit was measured by the degree of dependence upon mechanical support to maintain respiratory function. The range is from no dependence to almost complete dependence on a 24-hour basis. Five levels were used based on a system developed by Spencer.[5] They are (1) independence of support; (2) occasional dependence (e.g., when an infection interfered with respiration); (3) mechanical support only at night; (4) support for 12 to 18 hours a day; (5) support for more than 18 hours a day. People were asked during the interview to rate their respiratory status as it was one year after they developed polio and as it was at the time they took part in the study. In addition, they were asked in which year they felt they had reached their "best" or their "worst" levels of respiratory status. (For the majority [77%] the lowest level was one year after onset and most had achieved their optimal level five to six years after developing polio [87%], a level which they continued to maintain.) The clinicians used the medical records to assess what each individual's respiratory status had been one year after onset.

Measures of Mobility and Activities of Daily Living

Both the questionnaire used with the nonrespiratory sample and the interview schedule used in the research on respiratory polio included a battery of individual items and summary scales to measure mobility and self-care activities. On each question,

people were asked to rank their ability to perform the function on a five-point scale: (1) independent performance with ease; (2) independent performance with difficulty; (3) dependence upon equipment; (4) dependence upon equipment and people; (5) complete inability to contribute in any way to the performance of that particular mobility or self-care function.

The mobility index developed for the initial respiratory study consisted of eight basic mobility functions. These included bed and chair transfer, mobility on a level surface, the ability to manage stairs and mobility out of doors in winter and in summer. (The Manitoba climate makes this a pertinent distinction.) Because mobility depends upon the ability to use transportation systems, three other functions were added to the list: the ability to ride in transport specially designed for the disabled and to ride in or to drive a car. People using portable positive pressure breathing equipment can manage the first, but not the second or third; others can ride in a car, but have insufficient use of their upper limbs to drive it.

A modified version of Katz's "Index of Daily Living Schedule" was used.[6] It was augmented by questions on the ability to turn door handles or to lift objects above the head. These were to measure the effects of polio on upper limb movements. Other questions were added to measure performance of more complex daily living activities such as shopping, cooking and cleaning.

In addition to completing these banks of individual items making up the mobility and Activities of Daily Living scales (ADL), people used the same five-point ranking system to make an overall assessment of both their mobility and ADL status. They were asked how they would assess their current capacities, their capacity at one year after onset and when their mobility and ADL had reached their "best" and their "worst" levels. (Given the current concern with aging and polio, it should be noted that 14% of the respiratory sample said that mobility and ADL had declined within the previous ten years.) The clinicians responsible for the medical record audit used the same ranking systems when assessing mobility status and ADL at one year after onset.

The third section of this paper will present some of the comparisons made between how individuals remember their condition as it was in the past and how the same condition was recorded

in their medical record. Comparisons will also be made between current status and status one year after onset. Before presenting these analyses, we will discuss what people taking part in the Manitoba study said about the processes of recalling their past experience when they first developed polio.

The questionnaire sent to those with nonrespiratory impairment asked whether they thought they could recall the most significant features of their experience during their first months in hospital: 45% thought they could recall most things that happened to them, 25% were less confident, and 29% said they could remember little or nothing from that period. Age at onset was the major factor determining how much people said they remembered, but the seriousness of their condition, the length of time in the hospital and the degree of residual impairment were also involved.

The questionnaire also asked whether information had come from others who had been involved during the acute and early rehabilitation phases of their illness. Fifty-five percent said that in recalling the early phases of their illness, they had used information provided by other people. Parents were most often named as informants by 45% of the nonrespiratory group, 5% referred to a spouse and 2% listed siblings or other family members. (Physicians were only occasionally named as information sources.) These data suggest that recollection data are not simply what people remember for themselves; they are a composite of what people directly recall from that period plus a series of anecdotes told them by others which they have incorporated into their version of the past.

Section Three

Validation of Retrospective, Self-Reported Measures of Functional Status

In a preliminary attempt to assess the convergent and discriminant validity of retrospective measures of functional status (i.e., respiratory status, mobility and performance of ADL functions) drawn from questionnaires, correlations between these indices and clinical audit measures were computed. (Medical record audit data for ADL functions did not exist because functional ability indices were not systematically used until 1960.) In con-

sidering these correlations it should once again be noted that all measures were based on identical five-point scales. This consistency in the measurement of functional status across methodologies is important in that it allows for a metrically unambiguous comparison of the correlations among the indices. Inspection of the correlation matrix shown in Table 1 indicates that the medical record audit-based ratings of respiratory status were most highly associated with the self-reported recall-based measures of respiratory status from the patient interview. Measures of mobility from the medical record audit were associated with interview-based measures of mobility and ADL performance to about the

Table 1. Medical Record Audit/Interview Disability Measure Correlations (Respiratory Follow-up Study)

		Medical Record Audit-Based Assessments of Functional Status	
		Respiratory Status (1-yr Post-Acute)	*Mobility (1-yr Post-Acute)*
	Respiratory status		
	One-year post-acute	.83	.64
	1980	.83	.61
Self-reported functional status from interview	Mobility		
	One-year post-acute	.59	.73
	1980	.64	.71
	ADL*		
	One-year post-acute	.68	.75
	1980	.74	.72

All correlations are significant at the $p < .01$ level.

*Medical assessments of ADL performance were not available from the full sample of respiratory patients.

same degree. The later associations, however, were more pronounced than the correlation between the medical record audit-based measure of mobility and the interview-based measure of respiratory status.

Analysis of the correlations between self-reported, retrospective measures and medical record audit-based measures using case notes from the onset of disability provides tentative evidence for the validity of survey-based measures. In order to understand the factors which may account for the variations in self-assessed and record audit-based measures of all areas of functional status, cross-tabulations of the two measures were evaluated. These tables generally showed that discrepancies between self-assessed and record audit-based measures reflected differences of "degree" in terms of patients' recall of the number of hours of respiratory equipment dependence, or differences in degree of need for aids and helpers in mobility and ADL performance, rather than major disagreement about whether people were respirator-dependent or totally unable (or fully able) to perform self-care or mobility functions.

Correlations Between Post-Acute and 1980 Measures of Functional Status

In the comparison of the medical record and interview-based measures of functional status for the one-year post-acute and 1980 measurement periods (Table 1), we found that there was little difference between the magnitude of the 1980 interview-based one-year post-acute record audit-based relations and the one-year post-acute (interview-based)/one-year post-acute (medical record audit-based) correlations. This pattern would, in fact, be expected given our overall finding that there were no dramatic shifts in the relative levels of functional status or overall disability levels among respiratory patients over the 20-30 year period between the one-year post-acute measurement and the 1980 questionnaire.

Intercorrelations Between Measures of Alternative Dimensions of Functional Status

A second dimension in evaluating the validity of questionnaire-based measures of disability relates to the concept of convergent or concurrent validity involving comparison of

several alternate measures of a concept to identify dimensions of an instrument that are highly intercorrelated or that provide unique information. Table 2 shows the correlations between the three dimensions of disability reflected in functional status measures of respiratory dependence, mobility and ADL performance. The correlations between each of the interview-based measures would suggest that respiratory status, mobility and ADL performance represent highly correlated dimensions of overall functional capacity of residual disability among respiratory polio patients. Consistent with conceptual expectations and supportive of the measures' validity is the fact that respiratory status emerges as a somewhat distinct measure, with mobility and ADL performance exhibiting the greater association.

Table 2. Correlations Between Primary Functional Status Measures (From Respiratory Patient Follow-up Interviews)

	Respiratory Status		*Mobility*		*ADL*	
	One-Year Post-Acute	*1980*	*One-Year Post-Acute*	*1980*	*One-Year Post-Acute*	*1980*
Respiratory status						
One-year post-acute	—	.83	.62	.66	.69	.74
1980	—	—	.61	.70	.65	.78
Mobility						
One-year post-acute	—	—	—	.78	.78	.71
1980	—	—	—	—	.67	.85
ADL						
One-year post-acute	—	—	—	—	—	.80
1980	—	—	—	—	—	—

Section Four

Evaluating Aging Effects in Functional Status Measurement

Initial univariate analyses designed to examine the relationships between age, sex and the health status variables are presented in Table 3. As indicated, age was significantly related to all three health status variables with respect to 1980 levels. For one-year post-acute levels, generally weaker associations with age were observed. Specifically, although age was significantly related to one-year post-acute ratings of mobility, only marginally significant relationships were found for ratings of respiratory status and ADL. With respect to sex effects, only the mobility ratings of men and women differed, with males exhibiting higher levels of mobility compared to women. This sex difference was marginally significant for one-year post-acute ratings.

Paired t-test analyses of one-year post-acute and 1980 ratings suggested that for the sample as a whole there was a significant improvement in levels of mobility ($t = 9.03$; $df = 112$; $p < .001$) and ADL ($t = 7.21$; $df = 110$; $p < .001$). Only a marginally significant improvement in respiratory status ($t = 1.72$; $df = 111$; $p = .09$) was observed, however.

The self-reported functional status ratings for one-year post-acute levels are retrospective. Given the cross-sectional orientation of the survey design, the analysis of change in functional status over "time" is, in the present case, clearly limited to the more restricted notion of changes in health status as they were

Table 3. Pearson Correlation and t-test Statistics for Relationships Between Age, Sex and Health Status Variables

	Respiratory Status		*Mobility*		*ADL*	
	One-Year Post-Acute	*1980*	*One-Year Post-Acute*	*1980*	*One-Year Post-Acute*	*1980*
Age	r = .15*	r = .29***	.20**	.25***	.17*	.23***
Sex	t = .27	t = .72	1.93*	2.16**	1.15	1.02

*p ≤ .10 **p ≤ .05 ***p ≤ .01

perceived in 1980. Within the scope of this limitation, however, one-year post-acute ratings can be treated as a lagged variable in a longitudinal model. Accordingly, in the present analysis, stepwise multiple regression was deemed to be the most appropriate technique for examining the relationships between age, sex and the change in ratings of functional status for the one-year post-acute/1980 interval. A separate, although structurally similar, regression analysis was performed for each of the three functional status variables. For example, in the analysis of respiratory status, the dependent variable was the 1980 ratings. The independent variables, in terms of their order of entry into the prediction equation, were one-year post-acute ratings of respiratory status, followed by age and sex. This order of entry (i.e., entering one-year post-acute levels into the equations first) allows for an evaluation of the importance of age and sex as predictors of change in the ratings of respiratory status for the time period referenced. In addition to the main effects of age and sex, two-way interaction terms defined as the products of (1) sex X age, (2) sex X one-year post-acute respiratory ratings and (3) age X one-year post-acute respiratory ratings were tested for significance with controls for main effects. Similar analyses were performed for ratings of mobility and ADL.

With respect to main effects, sex was not related to changes in any of the three functional status variables. Age, in turn, was not related to changes in either mobility or ADL, but was associated with changes in respiratory status ($F = 9.75$; $df = 1,108$; $p = .002$) The negative correlation between changes in respiratory status and age ($r = -.23$; $df = 100$; $p = .02$) corresponding to this effect would indicate that age was associated with less improvement in respiratory status over time. This interpretation of the effect was considered most appropriate given the marginally significant positive shift in respiratory status cited above.

Test of the age X one-year post-acute interaction effect indicated that age was, in fact, differentially related to change in respiratory status as a function of one-year post-acute disability levels ($F = 10.54$; $df = 1,107$; $p = .002$). The correlations corresponding to this effect (Table 4) indicate that age was associated with less improvement in respiratory status only among individuals who were most disabled in terms of one-year post-acute ratings.

A similar age X one-year post-acute interaction effect ($F = 10.13$; $df = 1,106$; $p = .002$) was found for changes in ADL ratings. The correlations corresponding to this effect (Table 4) indicate that age was related to less improvement in ADL among the initially most disabled individuals. At the same time, however, the significant positive correlations between age and change in ADL among initially less disabled individuals would indicate that for this group, age was associated with more improvement in ADL ratings.

It is noteworthy that the age X one-year post-acute interaction effect was not significant ($F = .55$; $df = 1,108$; $p = .46$) for changes in mobility ratings. As with univariate effects, however, sex appeared to be an important consideration for explaining the variance of this variable, with the sex X age interaction effect emerging as significant ($F = 8.25$; $df = 1,108$; $p = .005$). The within-sex correlations corresponding to this effect indicated that age was associated with less improvement among men ($r = -.27$; $df = 65$; $p = .03$) but was unrelated to changes in mobility among women ($r = .23$; $df = .44$; $p = .12$).

This pattern of results indicates, then, that age has a significant main effect upon changes in mobility among men, but not among women. The analyses reported do not test for the possibility of a significant within-sex age X one-year post-acute interaction effect. Given the apparent importance of sex for understanding mobility ratings, a separate regression analysis was performed for the male and female subsamples in order to test for this ef-

Table 4. Pearson Correlation Coefficients for Relationships Between Age and Changes in Health Status Variables for High and Low One-Year Post-Acute Disability Levels

	Respiratory Status		*Mobility (Males)*		*ADL*	
	High Disability	*Low Disability*	*High Disability*	*Low Disability*	*High Disability*	*Low Disability*
Age	-.61***	-.13	-.41***	-.25	-.30***	.31**
N	28	84	33	34	65	46

**p ≤ .05 ***p ≤ .01

fect. For males, as previous analyses indicated, there was a significant main effect of age ($F = 10.89$; $df = 1,64$; $p = .002$) upon changes in mobility. In addition, however, the age X one-year post-acute interaction effect emerged as significant ($F = 4.24$; $df = 1,63$; $p = .04$). Inspection of the age/change in mobility correlations corresponding to this effect (Table 4) indicates a pattern similar to that observed for respiratory status and ADL. Specifically, age was related to less improvement in mobility among the initially more disabled group. For the female subsample, on the other hand, no significant main or interaction effects for age were found.

The correlations presented suggest that the association between age and change in the functional status variables is, for the most part, limited to those individuals reporting high initial disability levels. This observation, coupled with the fact that there was a perceived shift to less disability over the referenced interval, would suggest that this correlation pattern might be understood in terms of the difference in the variability of functional status changes for the initially low and high disability groups. More specifically, this correlation pattern might be attributed to the greater degree or variance of change (i.e., improvement) in health status for the high as compared to low disability groups. In order to test for this possibility, comparisons of the variance of changes in health status were made for initially low and high disability groups. These comparisons indicated that there were significant differences in the variances of changes in ADL ($F = 3.15$; $df = 64,45$; $p = < .001$) and respiratory status ratings ($F = 2.17$; $df = 83,27$; $p = .003$). This effect was not significant for mobility status of males ($F = 1.69$; $df = 32,33$; $p = .14$). In all cases, however, groups with initially high levels of disability exhibited a greater variance of change than did low disability groups.

Data collected for the sample of 527 nonrespiratory polio patients allowed for comparative analyses of mobility ratings. Univariate analyses of one-year post-acute and 1980 ratings indicated that there was a significant improvement in overall levels of mobility ($t = 11.51$; $df = 517$; $p < .001$). Age was associated with 1980 ratings ($r = .19$; $df = 523$; $p < .001$) but for this sample, there were no sex differences in mobility for either one-year post-acute ($t = .54$; $df = 515$; $p = .59$) or 1980 ratings ($t = .19$; $df = 527$; $p = .85$).

Regression analysis for the sample of nonrespiratory patients indicated that changes in mobility were significantly related to age ($F = 67.86$; $df = 1,509$; $p = < .001$), but were not associated with sex ($F = .83$; $df = 1,509$; $p = .36$). Tests for interactions indicated that neither the sex X age ($F = .09$; $df = 1,508$; $p = .76$) nor the sex X one-year post-acute mobility ratings ($F = 2.75$; $df = 1,508$; $p = .10$) effects were significant. However, the age X one-year post-acute mobility rating effect was highly significant ($F = 145.73$; $df = 1,508$; $p < .001$). Within-sex analyses suggested that this effect was more pronounced among men ($F = 126.90$; $df = 1,279$; $p < .001$) than among women ($F = 43.14$; $df = 1,225$; $p < .001$). The zero order sample correlation indicated that age was associated with less improvement in mobility ($r = -.22$; $df = 511$; $p < .001$). Here again, however, this association was only significant among the initially more disabled group ($r = -.58$; $df = 77$; $p < .001$) and not among those with relatively high initial levels of mobility ($r = .03$; $df = 412$; $p = .60$). As in the analysis of the respiratory sample, this effect was attributable to a significant difference in the variance of changes in mobility ratings ($F = 5.55$; $df = 79,415$; $p < .001$) between the initially high and low disability groups.

Summary

Our experience in developing follow-up studies of populations of respiratory and nonrespiratory poliomyelitis patients has demonstrated the feasibility of applying epidemiological approaches to the study of post-polio aging. We have found that it was possible to apply a historical prospective approach to document the experience of a representative population from the point of disease onset and thereby control for selection bias and recall artifacts inherent in cross-sectional studies of self-selected groups of survivors. To facilitate cumulative research, we advocate the development of comparable measures of functional status that are based on widely accepted indices of ADL performance, respiratory status and mobility. In our evaluation of the validity of retrospective, self-reported measures of functional status, through comparison with data on post-acute status from the medical record audit, we found a high degree of correlation between the two overall measures. Finally, our preliminary attempts

to evaluate post-polio aging effects indicate that age at onset was significantly correlated with changes in functional status variables. This association is apparently a function of initial disability levels.

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Poliomyelitis in Denmark

Ellen Errebo Larsen

Denmark is a small country with a population of slightly over 5 million. Being part of Scandinavia, we have often shared the epidemiological fate of our neighboring countries, Norway and Sweden. The first Scandinavian descriptions of poliomyelitis were of epidemics in Sweden in 1801 and 1807. At that time the disease was practically unknown, and attention focused on the paralytic aspect. The first major epidemics occurred notably in Scandinavia. It is not surprising, therefore, that Norwegian and Swedish epidemiologists were pioneers in polio epidemiology research.

Oskar Medin (1847-1927) delivered a lecture in 1891 on several epidemics in Sweden and published in 1896 a survey of accomplishments in polio research. Medin was convinced that polio was an infectious disease. Like many other epidemiologists he made the observation that the disease notably hit otherwise healthy children and that the incidence of polio, contrary to many epidemic diseases, was not particularly high in the poorest population groups. Therapeutically, he found that antipyretics had no influence on the course of infection.

Another Scandinavian doing research on polio was the Norwegian Christian Legaard (1851-1921). In a major article published in 1909, he reviewed over 1,000 cases in a large epidemic in Norway in 1905. He was one of the first to point out that in many aparalytic and abortive cases the diagnosis of polio could only be established because they occurred during an epidemic. He believed that the disease was often spread by such cases. This theory was confirmed some years later.

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During the period 1908-1911, after several foreign researchers had demonstrated the infectious agent by transmission to monkeys, four major polio epidemics occurred in Sweden. They were described by Wernstedt (1872-1962) who demonstrated that in rural districts the disease rarely occurred in the same area more than once during a five-year period. This is, of course, easily explained by the immunity of the population group which had been exposed to infection. On the other hand, in urban areas it was not unusual that epidemics occurred year after year. Wernstedt found that mortality was lowest in the 0-5 age group and that it rose with age, but only 24% of his cases were over age 15. Wernstedt advocated active therapy. In his opinion, training of paralyzed patients should be initiated at an early stage by active and passive exercise and contracture-prophylactic treatment.

In contrast to this method of approach the treatment generally recommended in the 1920s and 1930s was immobilization with braces, splints, frames and casts to avoid contracture of affected muscles and of the spine in the hope that rest would expedite cure of the inflammation of the gray matter of the spinal cord. It was considered beneficial for paralyzed muscles to be protected and that they should not be exposed to active exercise until after some weeks of complete immobilization.

In the 1940s this reasoning was sharply criticized by Elizabeth Kenny (1886-1952). She found that paralyzed muscles should not be immobilized but trained as soon as possible after the onset of the disease. Accordingly, she counteracted muscular spasms by heat and encouraged patients to move the nonactive muscles in which nerve impulse had been preserved but not utilized. Her method was introduced in Denmark in the 1940s.

In Denmark there were no major epidemics until 1934. During the period 1910-1933 only four minor epidemics with a maximum of 389 cases were recorded; however, 1934 saw an epidemic with over 4,500 cases. Since then, paralytic as well as aparalytic cases have been registered.

As will be seen from Table 1, Denmark experienced its largest epidemic in 1952. The vast majority of cases occurred in Copenhagen whose population at that time was approximately 1 million. This event spurred epidemiological studies which ensued in the theory that infection causing paralysis is notably transmitted by children, while infection transmitted by persons over age 5 often

Table 1. Number of Reported Cases of Acute Poliomyelitis in Denmark

	Paralytic	*Aparalytic*
1934	ca. 600	4111
1935	107	291
1936	30	49
1937	546	697
1938	288	278
1939	41	57
1940	10	13
1941	256	335
1942	616	666
1943	27	270
1944	1019	902
1945	235	595
1946	58	132
1947	99	406
1948	408	520
1949	153	170
1950	308	1963
1951	20	363
1952	2450	3226
1953	695	896
1954	72	280
1955	24	46
1956	37	154
1957	10	16
1958	65	29
1959	11	16
1960	4	18
1961	140	216
1962	10	5
1963	6	

takes a symptomless course, at the same time producing resistance.

As shown in Figure 1, which depicts the weekly influx of poliomyelitis patients admitted to the isolation hospital in Copenhagen, the number of cases rose steeply during August and September 1952 and the vast majority of victims were children.

In 43% of the persons admitted to the hospital the paralyses

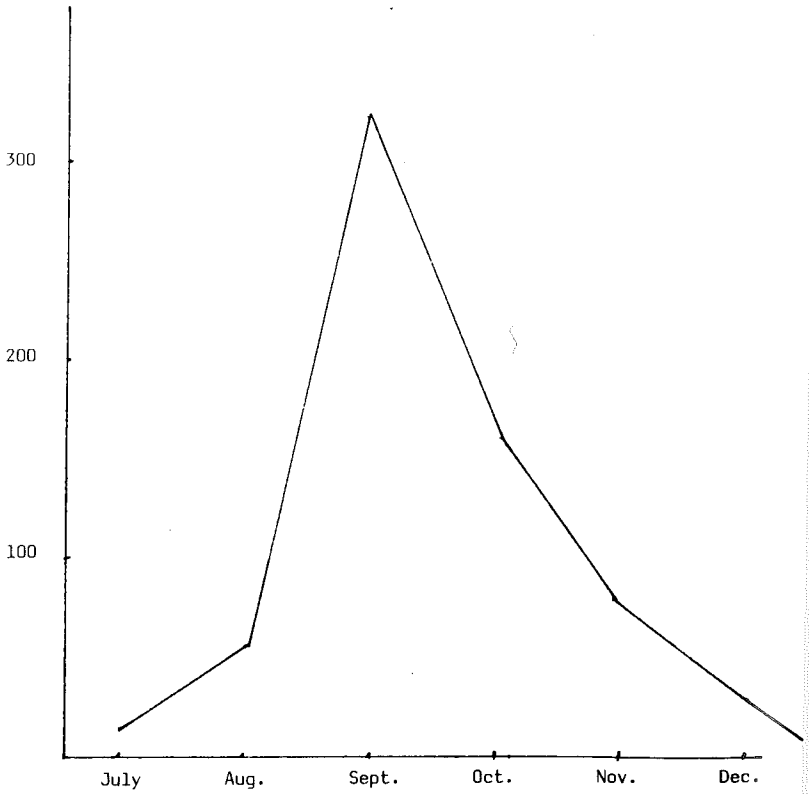

FIG 1. The weekly accession of acute poliomyelitis at Copenhagen's epidemic hospital in 1952.

were permanent. They received follow-up treatment, most of them in the Polio Society's outpatient clinic which, in addition to providing training, handled social problems as well as educational problems for children.

The Polio Society was founded in 1945. Its primary objectives were, and still are, to support the fight against polio and to treat and help polio victims. The Outpatient Clinic for Physiotherapy was established the same year. At a very early stage the Society set for itself the goal to rehabilitate the largest possible number of polio victims, to help them to the greatest extent

possible to become self-sufficient and resume an independent life in general (adaptations to their homes, provisions of aids, motorization) and at work (work capacity testing). After the major epidemic in 1952 the capacity of the Clinic was expanded, and it has since provided treatment for a very large number of patients with paralyses.

The number of treatments given to persons with severe motor handicaps, notably polio victims, is now 22,000 annually. Treatment consists predominantly of exercises, including walking exercises, training to promote self-sufficiency and instruction in the use of aids. In addition, great emphasis is placed on stretching tight muscles, joint capsules and tendons.

Some patients receive permanent conservative treatment where possible in teams. Furthermore, there are facilities for training in a swimming pool, a form of treatment which is considered to be of great value for highly immobile patients. In addition, persons exhibiting symptoms of overtaxing, often attended with pain, are treated with packs, massage, ultrasound, short wave diathermy and diadynamics. For relaxation, biofeedback is applied.

The Society has made a nationwide follow-up study which resulted in the registration of 3,650 patients. It is presently estimated that there are about 8,000 polio victims in Denmark. The purpose of the follow-up which took place from 1976 to 1984 was to offer assistance to polio victims faced with either medical or social problems, to arrange for adaptations to their homes and to assist in filling out and recommending applications for aids, motorization and social services. Where State-provided support is considered to be inadequate, the Society is able to provide financial help.

Following mass vaccination in the 1950s and 1960s there have been few cases of polio in Denmark. All the new cases referred to the Clinic for treatment occurred in immigrant children. We believed, therefore, that the number of polio patients requiring treatment would drop in step with the decline in their numbers. But this was not the case. The past ten years have seen a rise in the number of persons referred to the Clinic for help. We have compiled statistics on this recent influx, and it appears that the majority of the patients concerned are between the ages of 40 and 50, i.e., those who were children in 1952.

The new patients we see often have social problems. They have difficulty in overcoming troubles which they were previously able to cope with at work or in private life. At examination, the patients complained of general weakening of muscles and pain in joints and muscles.

Objective examination revealed typical symptoms of overtaxing and degenerative changes in the form of arthrosis, myoses and tendinitis at the site of tendon-muscle attachments. These changes were often seen in extremities without pareses or in the spine and dorsal muscles which have constantly been overtaxed because of scoliosis stemming from shortening and paralysis of one leg.

Degenerative changes were frequently seen in shoulders, elbows and root joint of the first finger in patients having used ordinary sticks or crutch-handled sticks for many years.

Another disorder causing great inconvenience to many polio patients is poor circulation in paralyzed muscles. This produces an unpleasant sensation of cold which, of course, is accentuated when the affected extremities are exposed to cold. The patients have difficulty in moving outdoors in cold winter weather, and starting out in a cold car is also a strain.

In step with the progressive weakening of paralyzed muscles with age and wear and tear, the patients become increasingly immobile. They have mounting difficulty in walking and many have to use a wheelchair. This, in turn, gives rise to complications such as reduced mobility of joints and decubiti. As a result, many patients require more care, perhaps to the extent that they can no longer stay in their own homes but have to be placed under institutional care.

Therefore, it is of overriding importance to follow the performance of these patients very closely through conservative treatment once a week. This enables us to deal promptly with problems requiring special attention. Treatment required may be exercises aimed at preserving the level of self-sufficiency. Other requirements may be to relieve symptoms of overtaxing in muscles and joints, to provide the patients with appropriate supports, right type of sticks, right aids in the home and at the workplace and finally to assist in motorization. It is essential to make life easier for these patients and take care of their health if they are to have

a chance of being able to continue to function at the level reached through previous treatment and personal training.

It was remarkable to see in several of these patients that the muscles were weaker than at previous examination. This applied not only to paralyzed but also to previously healthy muscles. Over the years we have seen so many cases of increasing weakness in the 40-50 age group that we realize that this is not a haphazard occurrence. We have succeeded by training to restore these muscles to some degree of previous strength. Therefore, we make a point of keeping the patients in conservative training once a week which, in our experience, is extremely beneficial.

Clinical Management

Strengthening Exercises in Normal Muscle

Gerald J. Herbison, M.D., M. Mazher Jaweed, M.S. and John F. Ditunno, Jr., M.D.

Introduction

Exercise has become an integral part of our life style. An increasing number of individuals jog, play tennis or racquetball, swim, bicycle and engage in various other sports activities. Emphasis in the past has been on endurance activities; however, with the increasing interest in strengthening and bodybuilding there has been an upsurge of scientific studies aimed at determining the physiologic consequences of weight lifting.

Although the present symposium is devoted to the late effects of polio, it is helpful to identify the results of strengthening activities in normal subjects to better understand its consequences in muscles weakened by poliomyelitis.

Definitions

Force is equal to mass times acceleration. However, for the purposes of this discussion, it is simply the load, weight or mass supported by an extremity. Work is defined as force times distance. Thus, if a one pound weight is lifted one foot, the work is equal to one foot pound. Power is equal to the mass or weight lifted times the distance over which the load is lifted divided by the time interval over which the force is lifted. Thus, power is equal to force times distance over time. Some individuals[1] have

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stated that the use of the word power has been grossly misused in physiological literature.

Static contractions are defined as isometric contractions or contractions where the external work is equal to zero; the extremity supports the weight without moving the joint through an arc. Dynamic contractions are of two types: isotonic and isokinetic. Isotonic contractions are either concentric or eccentric; the former being a shortening contraction, the latter a lengthening contraction. A shortening contraction results from lifting a weight through a range of motion, thus shortening the distance between the origin and insertion of a muscle. On the other hand, a lengthening or eccentric contraction results from a force being excessive enough to lengthen a muscle during contraction such that the distance between the origin and insertion of the muscle increases. An isokinetic contraction is defined as a contraction where the velocity remains unchanged.[2] A more understandable definition of an isokinetic contraction is one where the muscle shortens and the external force applied to an extremity is identical to the force of muscle contraction. In a sense an isokinetic contraction is a subcategory of an isotonic contraction. Both an isokinetic and an isotonic contraction can move an extremity through a range at a constant velocity; however, with an isokinetic contraction the external force applied exactly counterbalances the force exerted by the muscle.

A power or weight lifter increases the force or load lifted by performing a few brief contractions several times a week. Bodybuilders, on the other hand, increase their muscle mass and at the same time they increase their force of muscle contraction. Tesch and Larsson[3] have stated that bodybuilders perform 6 to 12 contractions until concentric contractions fail and then repeat these contractions approximately 20 times within a half-hour period. Obviously, this is a different type of contraction than a single maximal contraction which cannot be repeated because of the magnitude of the external force lifted.

Physiologic Response to Strengthening Activities

With the above definitions as a background, the following presentation will identify the gross and microscopic changes resulting from various types of exercise programs, the reasons

they occur and the type of exercise programs that may contribute to an increase in strength.

Any voluntary contraction greater than 65% of maximum performed three to six seconds, three to five times a day, two to five times per week at any angle will increase strength. The percent increase in strength is greater than the percent increase in muscle fiber area.[4]

The strength increases with any type of exercise program independent of whether that exercise program is isometric,[5] isokinetic[6] or isotonic.[7,8] However, there is an indication that there is some degree of specificity.[9]

One of the most interesting aspects of any muscle strengthening program is the ability of the individual to increase the force of contraction independent of age in the absence of an increase in cross-sectional muscle area. Moritani and deVries[10] demonstrated a 30% increase in strength over an eight-week period of time in 18- to 26-year-old individuals and 67- to 72-year-old people with a two-thirds maximal isometric contraction performed ten times, two times per day, three times per week. Where the younger individuals increased their extremity circumference, the older individuals had no evidence of an increase in muscle bulk. Similarly, MacDougall et all[11] demonstrated that an isokinetic program of three second maximal contractions repeated ten times per day increased the force of contraction 90%; however, the type 1 and 2 fiber areas increased 30% at the most. The large increase in the force of contraction and small degree of muscle hypertrophy[10] may be related to an increase in contractile protein content,[12] increased fiber numbers[13] and/or central nervous system adaptations.[14]

Gordon and his associates[12] exercised rats by having them climb a 16 inch ladder with weights equal to their body weight on a daily basis. Each rat climbed the ladder five times with a three-minute rest period between each bout. The animals exercised 25 times in the morning and 25 times in the afternoon. They demonstrated a marked increase in protein concentration with little increase in fiber size. This is consistent with an increase in myofibrillar protein content within each muscle fiber in the absence of any hypertrophy.

Power lifters and bodybuilders increase their strength. However, bodybuilders dramatically increase their muscle bulk.

Bodybuilders have demonstrated evidence of fiber splitting, central nuclei and fiber necrosis.[15] There is some thought that this represents an adaptive response to increase the fiber number. Gonyea and Sale[13] have demonstrated that repetitive weight lifting activities resulted in a 9% increase in fiber number. However, there is some disagreement[14] regarding the significance of this increase in fiber number.

The muscle damage noted above occurs more readily in lengthening contractions than in shortening contractions.[16] This is relevant to the discussions in the present symposium on the progressive weakness that is sometimes found some years after the acute onset of polio. For a given force of contraction reportedly the number of motor units is much less for lengthening than a shortening contraction.[17] This suggests that damage may occur if the intensity of contraction is excessive in relation to the number of motor units. Expressed as an equation ($D \propto I.R./NMU$) damage (D) is directly related to the intensity of contraction (I) multiplied by the repetitions performed by the muscle (R) and divided by the number of motor units (NMU). For a given load, an instantaneous lengthening contraction utilizes fewer motor units than a shortening contraction. The disproportionate stress on the muscle fibers may contribute to inflammation and necrosis.

Many investigators have attempted to demonstrate that one type of exercise program is more beneficial than another. Darcus and Salter[8] compared isotonic to isometric strengthening activities and found that there was a similar increase of strength in both the exercise programs. They did not perform any type of cross-over experiment. Liberson and Asa,[5] on the other hand, compared isometric to isotonic activities in a cross-over study utilizing the Oxford program.[18] One group of individuals performed a progressive resistive exercise (PRE) program and a second group an isometric program. The isotonic group performed ten repetitions at 50%, ten repetitions at 75% and ten repetitions at 100% of the ten repetition maximum. A second group of subjects performed 20 6-second maximal isometric contractions. The isometric program increased the force of contraction more than the isotonic when tested either isometrically or isotonically. It should be noted than even with ten maximal isotonic contractions, the total duration of the maximal contrac-

tion is relatively brief compared to six 20-second maximal isometric contractions.

Finally, Thistle et al[6] evaluated an isokinetic exercise program. The individuals performed ten repetitions of isokinetic activities four days per week for eight weeks. They found a 40% increase in isokinetic strength with a 10% increase in the isometric force and a 30% increase in the isotonic contraction. They did not perform a cross-over-type study. In summarizing these experiments, it appears that independent of the exercise program the strength increases. As yet, there is not a single study that has adequately demonstrated the superiority of one exercise program over another.

Although there has been some criticism of Hettinger's[19] work[4] on isometric training, certain principles are exemplified by his study more than any other study. He evaluated four separate groups of subjects who increased their isometric strength 30%. One group of subjects performed a 65% maximal voluntary contraction while the remaining three groups contracted at 100% of maximum voluntary contraction. The group that contracted at a 65% maximal force for one second once a day required eight weeks to increase the strength 30%. Subjects who contracted at 100% maximal voluntary contraction for one second one time per day required six weeks to increase their strength 30%. Individuals who contracted at 100% maximal voluntary contraction for six seconds one time per day increased their force of contraction 30% over a five-week period. Finally, the group that performed 100% maximal voluntary contractions for six seconds five times per day required four weeks to increase their strength 30%. They found that it made little difference whether the number of seconds or number of times the contractions were performed was increased. Little benefit accrued from increasing the force of contraction to more than six seconds or five times per day. His findings have considerable significance for clinical medicine. Many individuals cannot contract their muscles more than 65% of maximum voluntary contraction because of cardiac, pulmonary, arthritic or psychologic conditions. Yet these individuals benefit from an increase in strength. There are no studies that demonstrate that the strength increases with a training program of less than 60% of maximal voluntary contraction.[4] Studies demonstrate that 3- to 6-second contractions performed

two to five times per day approximately two to three times per week sufficed to increase strength.[4] It should be noted that although it is possible to increase strength with one contraction per day, the strength increases most rapidly when the exercise is performed every day at 100% of the maximal six seconds voluntary contraction repeated five times per day on a daily basis.[19]

There has been some controversy regarding the angle at which an individual should perform isometric contractions.[20] Stillwell et al[20] found that the isometric force of contraction increased independent of whether the quadriceps was maximally contracted at 30% or 60% of knee flexion. This is important because some patients are unable to forcefully contract at all angles.

Finally, there has been a recent study evaluating the effects of electrical stimulation. Laughman and associates[21] among many others have demonstrated that tetanic stimulation increased the force of contraction 20% which was similar to a voluntary strengthening program. It is imperative to determine, however, whether an individual should be subjected to electrical stimulation to increase the force of voluntary contraction if the same increase in force can be obtained with a voluntary contraction.

Summary

An exercise program aimed at eliciting a force of contraction greater than approximately two-thirds of maximal voluntary contraction performed three to six seconds three to five times per day two to three times per week at any angle will increase strength. The increase in strength of contracton is about three times greater than the increase in extremity circumference and fiber area. The increase in strength is due to an increase in the central nervous system adaptions, protein concentration, muscle fiber hypertrophy and fiber number. The strength increases in any type of exercise independent of whether it is isotonic, isometric or isokinetic. The type of exercise program should be tailored to the needs of the patient.

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Clinical Management of Partially Innervated Muscle

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Introduction

Follow-up data on the late effects of polio indicate that 22.4% of individuals who had paralytic poliomyelitis experienced deterioration of strength since their maximal recovery from polio (Mary Codd et al, this volume). Sixty-six percent of the subjects worsened in the severely involved muscles along with 15% new weakness in formerly normal muscles.

The loss of strength can be explained on the basis of a slow progressive loss of anterior horn cells,[1,2] age-related decrease in the force of contraction[3] superimposed on weakened muscles, disuse (Richard Owen, this volume) and exercise-induced damage of the motor unit.[4]

The purpose of this presentation is to discuss exercise-induced muscle weakness because it may be prevented. We will discuss activities that may be harmful, not helpful and beneficial in managing patients with progressive late onset weakness who had polio.

Activities That May Be Injurious to Patients

As early as 1917, Lovett[5] described patients who developed progressive weakness after performing farm activities such as milking cows on a daily basis. Bennett and Knowlton[6] caution-

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ed against excessive exercises because of their potential harm to partially innervated muscles. It may be argued that some of their patients weakened because of concomitant medical problems. One of their patients developed progressive weakness of the thenar muscles during pregnancy. This patient might have had carpal tunnel syndrome which was not excluded in the clinical work-up. Nevertheless, it is difficult to explain the progressive weakness noted in their other patients or in the patients described by Mitchell[7] and Hyman,[8] since other causes of progressive weakness were ruled out. Moreover, it is unlikely that the loss of strength was due to aging because all the patients were young adults. Drachman et al[9] reported nine patients who had polio several years prior to the time he biopsied their weak muscles. These patients demonstrated a wide variation of fiber size, central nuclei, fiber splitting and fiber necrosis. He suggested the myopathic findings represented a compensatory mechanism to increase the muscle fiber number. Reitsma[10]and Van Linge[11] overworked rat plantar flexor muscles by eliminating their synergistics. The fiber splitting, central nuclei and fiber necrosis they found were thought to result in an increase in the force of plantar flexion contraction. Armstrong et al[12] demonstrated fiber splitting, centralized nuclei, fiber necrosis and phagocytic infiltration after multiple lengthening contractions of normal muscle. It is well known that shortening contractions cannot generate the same force of tension as eccentric contractions. Therefore, for a given force of contraction fewer fibers are required to produce the contraction eccentrically than concentrically.[13,14] Tesch[15] and Armstrong[12] felt that the reduction in the overall number of muscle fibers contributing to a given force of contraction eccentrically damages the muscle fibers and leads to fiber necrosis, central nuclei fiber degeneration and mononuclear infiltration.

The above clinical and experimental phenomena suggested to us a relationship between muscle damage, intensity of exercise, the time over which the exercise is performed and the number of motor units.[4] We hypothesized that damage is directly related to the intensity of exercise and the time over which the exercise is performed and inversely related to the number of motor units contributing in the force of contraction.

To test this hypothesis we evaluated muscle at the time of

reinnervation and shortly thereafter.[16-18] We found that the myofibrillar protein content increased when the overwork was initiated three weeks after nerve crush. However, it decreased when it was initiated two weeks after nerve crush. This tends to corroborate our hypothesis that damage is inversely related to the number of motor units. Presumably, two weeks after crush denervation fewer motor units contributed to the force of contraction than at three weeks after crush denervation. We subsequently performed a similar type of experiment: however, rather than eliminating synergists we swam the animals.[19] When the animals were exercised four weeks after nerve crush, there was a greater protein content than when the swimming was begun three weeks after nerve crush. This supports our hypothesis that overwork initiated in the absence of sufficient motor units may contribute to damage.

Nerve crush results in such rapid nerve regeneration that we selected a model that would limit reinnervation. Therefore, we partially sectioned the sciatic nerve by removing 70% of the axons.[20] Immediately thereafter, we subjected one group of animals to two hours of electrical stimulation, the second group to four hours and the third group to eight hours of electrical stimulation. The electrical stimulation program consisted of 10 Hz stimulation which is subtetanic. Utilizing this protocol we found that independent of the duration of electrical stimulation, all animals increased their muscle weight and tetanic tension. This very mild electrical stimulation was interpreted as being less vigorous than the exercise utilized in the previous experiments where the muscles were overworked either by performing synergistic tenotomy or swimming. Therefore, although the number of motor units was reduced, the activity was mild. Thus, damage did not occur. The results of the study suggest that regeneration was facilitated by two, four and eight hours of electrical stimulation of the sciatic nerve. Hoffman[21] suggested that low intensity electrical stimulation of the nerve facilitated peripheral sprouting. This may be the reason for the increase in muscle weight and tension in the electrically stimulated animals compared to the partial nerve section control animals. Another explanation is that the denervated muscle fibers were stretched which partially limited their atrophy[22] (McComas, personal communication). We do not believe the innervated muscle fibers

hypertrophied from the electrical stimulation because there was no evidence of hypertrophy of normal muscle after stimulating its nerve supply with the sound current intensity mentioned above.

Since we were primarily interested in determining whether overwork would damage muscle, and because of the necessity of developing a model that would remain permanently denervated, we elected to avulse the L5 root. Root avulsion of L5 results in approximately 80% denervation of the soleus muscles (unpublished data). Ten days after root avulsion, we performed synergistic tenotomy of the gastrocnemius and plantaris muscles or exercised the animals for one hour at an 8% or 35% grade at one mile per hour. The animals were sacrificed 24 days after root avulsion. There was no evidence of any wide variation of fiber size, central nuclei or fiber necrosis in the exercised muscles. In each instance, the number of small fibers was significantly greater in the overworked muscles than in the L5 control muscles. The small fibers were similar in fiber area to those found in denervated muscle. Although we had initially hypothesized that overwork may damage muscle directly, it appeared that the overwork may have inhibited reinnervation.

The root avulsion may have caused damage to the spinal cord. Therefore, we sectioned the L4 and L5 nerve roots and subjected the soleus muscles to overwork by tenotomizing the gastrocnemius and plantaris muscles. Elimination of synergistic muscles results in a marked hypertrophy[23] and an increase in tetanic tension[24] in normal soleus muscles. With L4 and L5 spinal nerve section done at the same time as synergistic tenotomy, there was no evidence of either an increase in muscle weight or tetanic tension of the soleus.[25] This suggests that exercise is futile for markedly denervated muscles, since they are overworked from the elimination of synergistic muscles due to the partial denervation.

In summary, it appears that damage may occur from multiple contractions performed over a period of time. If a patient complains of fatigue or progressive weakness, it would seem reasonable to support the muscle with appropriate splinting and/or to decrease the level of activity to determine if such a program restores strength.

Approaches Not Considered Helpful

In the previous discussion, we outlined reasons for cautioning patients against the overwork of weak muscles. We will now discuss therapeutic approaches thought to be of little value for increasing the strength of denervated muscle. Although stretching is beneficial in maintaining the range of motion, there is no evidence that passive range of motion contributes to an increase in strength. Stretching denervated muscle increases its weight by the addition of sarcomeres in series.[26,27] In one report Ashmore and Summers[28] stated that passive stretch of the muscles increases the fiber area. However, this was demonstrated on innervated muscle. The animal may have fought against the immobilizing device and hypertrophied the muscle isometrically. Studies indicate that where passive tension does not prevent a loss of contractile protein concentration in denervated muscle, active tension elicited by electrical stimulation limits its decline after sectioning the nerve.[29] Although electrical stimulation of denervated muscle retards atrophy,[30] there is no proof that it enhances reinnervation of totally denervated muscle.[31] Long duration galvanic currents are required for activation of denervated muscle. This type of current is more painful than short duration currents. It is difficult, therefore, to subject a patient to tetanic contractions using long duration currents. If simple twitch contractions are prescribed, the force of contraction is at best one-fourth of tetanic tension. Hettinger[32] showed that anything less than 20% of the maximal voluntary contraction does little to maintain strength. Finally, the current must be increased greatly to stimulate all the muscle fibers from the surface of the muscle to the bone. This increases the chances of noncompliance. It has been shown that the current density drops off precipitously from the surface to a few millimeters below the surface.[33] Therefore, unless the current is increased, only the superficial muscle fibers will be activated.[34] In summary, there is little question that optimal electrical stimulation programs retard atrophy. However, in the two studies that have been performed on humans, there has been no evidence of improved reinnervation with chronic electrical stimulation.[35,36] It seems pointless to perform electrical stimulation on totally denervated muscle if reinnervation is not

anticipated or if reinnervation is not improved by chronic electrical stimulation. There may be, however, an indication for performing electrical stimulation in partially innervated muscle, since it has already been shown that high frequency tetanic stimulation can increase the strength of normal muscle.[37] This increase in strength is no more than that achieved through normal voluntary contraction. If an individual is unable to perform maximal voluntary contraction, then chronic tetanic electrical stimulation may be of some benefit.

Approaches That May Be Beneficial

We will conclude by discussing approaches that may be beneficial to partially innervated muscle. Cooling reduces muscle power. An increase in ambient temperature might increase a patient's force of contraction.[38] The use of appliances to minimize overstretching of the muscle connective tissue might contribute to optimizing the force of contraction.[39] If the connective tissue is overstretched, the force of muscle contraction may eliminate the laxity in the connective tissue, but not contribute to joint motion. Therefore, it may help to splint joints until the motor power is strong enough to support multiple contractions.

Brief isometric contractions contribute to an increase of strength in partially innervated muscle. This was demonstrated by Russell and Fisher-Williams[40] who initiated brief forceful contractions two months after onset of polio and Muller[41] who similarly found an increase in muscle strength of partially innervated muscles in patients who had polio many years after the acute episode. This is consistent with the abovementioned hypotheses relating damage to the intensity of exercise, the time over which the exercise is performed and inversely related to the number of motor units. By utilizing brief maximal contractions of a few motor units, damage does not occur, but rather the force of contraction increases.

Functional bracing is indicated in the patient who has lost the capacity to activate a joint.[4] As stated elsewhere in this volume, there is a multiplicity of appliances which can assist in joint motion and respiratory function.

Finally, although surgical intervention is usually considered

for young patients, it may be advisable to consider utilizing simple procedures to improve function.[4]

Summary

The late onset of weakness after polio should be prevented by limiting overwork if there is an indication that it is contributing to the decrease in strength. There is no indication that electrically evoked twitch contractions are of any benefit in the management of denervated muscles. Finally, the judicious use of warm environments, brief isometric exercises, appliances and surgery may improve self-care, vocational activities and avocational endeavors.

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Post-Polio Pain: Treatment by Sublingual Immunotherapy

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Introduction

Discussion of the difficulties being encountered by post-polio patients is usually centered around progressive weakness and disability.[1,2] There are a few patients, however, who have had severe discomfort. This "post-polio" pain is different from that related to and expected from skeletal problems and is poorly controlled by the usual simple analgesics, including codeine. Antidepressant drugs also prove ineffective. The pain is difficult to localize and may be described as "bone," "muscle" or "nerve" pain, "like when I had polio." Although constant, it may be accentuated by exertion or illness. Headache is frequently present and may be severe. Insomnia and restlessness are additional complaints along with depression and frustration from absence of objective findings. The degree of weakness does not seem necessarily to be related to the severity of the pain nor is the pain confined to muscles known to have been injured by polio. Patients often have undergone extensive work-up including EMG, myelogram, EEG and CAT scan without definitive diagnosis, and many have been referred for psychiatric evaluation and treatment.

Because of the similarity of post-polio pain to that of herpes zoster,[3] and because of very good results in relieving pain of shingles by sublingual immunotherapy using influenza vaccine, attempts have been made during the past four years to relieve the pain of some of our polio patients by the same method, using Salk polio vaccine.

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Chart Review

On retrospective review of charts of 80 patients treated by immunotherapy, the patients were found to range in age from 24 to 71 at the time seen, with date of onset of polio from 1913 to 1961. Thirty-three were men; 47, women. Long-term residuals varied from apparent full recovery to severe weakness of the trunk and all extremities. Symptoms presenting from one to five years before evaluation included pain, increased weakness (often of previously uninvolved muscles), loss of endurance, headache and insomnia. Twenty patients had undergone extensive work-ups at other facilities without definitive diagnosis of cause of pain. Medications reported as ineffective included aspirin, other non-steroidal anti-inflammatory agents, proproxyphene, thioridazine, diazepam, amitriptyline, steroids (oral and injection) and codeine compounds.

Response to immunotherapy was reported to be good in 47 patients, with marked reduction in muscular pain, headache and/or fatigue, while 11 obtained no benefit from treatment and six had equivocal results. No follow-up information was available on 16 patients. No side effects were reported or noted with the exception of an increased incidence of fever blisters in one patient and increased fasciculations in another, both of whom gained good relief from pain. Response, if obtained, was immediate and could be maintained by continued use of sublingual drops at intervals as necessary for further control. While a few patients have reported improvement in strength and endurance after prolonged use of immunotherapy, muscle weakness does not seem to be affected by treatment.

Discussion

The mechanism of action of this method of immunotherapy is uncertain and its effectiveness is questioned by allergists in general.[4,5] It has proven very beneficial clinically, however, in relieving reactions to foods, pollens and contactants. This may possibly be explained by binding of receptors on lymphocytes to prevent the cross-bridging as needed to precipitate a reaction, according to recent findings. Another possible explanation of mode of action may be activation of suppressor lymphocytes by an as yet undetermined process. Treatment is based on the use of an "allergen blocking dose" by which a reaction is prevented by a specific concentration of the antigen in question.[6,7] For example, the symptoms of hay fever from ragweed pollen can be

controlled by a patient-specific concentration of ragweed pollen. The antigen can be administered either subcutaneously or sublingually with equivalent results.

The sublingual route has the advantages of excellent patient acceptability, ease of administration, no requirement for sterile technique and applicability to all types of allergens, including foods and contactants as well as inhalants and microbials. The "antigen blocking dose" for each allergen is specific and is determined by changes in pulse and temperature as registered after administration of each of a series of concentrations of the antigen in question. Reaction causes either an increase or decrease in pulse and/or temperature, and the relieving dose is identified by a return toward the norm. When the effective concentration or dose has been determined, symptoms are easily controlled by continued use as clinically indicated. As with removal of an antigen stimulus, over a period of time true desensitization may occur with no further need for therapy. Since only extremely dilute solutions of the antigen are used for testing, no drug effect need be considered. Allergic response is minimal, with no severe or anaphylactic reaction ever observed in over ten years of experience. Failure of previous efforts to establish reliability of sublingual therapy is probably due to attempts to determine the blocking dose by observation of symptoms rather than by objective measurements of pulse and temperature changes.

Some inferences as to the basic process causing the post-polio syndrome can be drawn from the response to immunotherapy. Although there is no evidence of activation of live virus with recurrence of actual infection, persistence of some viral element is suspected. A plausible explanation of the appearance of new problems might be the development of an abnormal immune response (an allergy) to the viral residue or viral template retained by the body to recognize a previously known invader. Such recognition is necessary to prevent reinfection, a response that enables permanent immunity. This may prove to explain the mechanism for many so-called "autoimmune" diseases.

Future Research

In consideration of the post-polio syndrome, a number of areas need to be explored. A double-blind study of the effectiveness of treatment by immunotherapy should be undertaken,

with objective findings from manual muscle tests and EMGs to substantiate patients' subjective reports of improvement. If results are positive, the mechanism of action of antigen blocking should be explored and correlated with recognized immune processes. Basic research is needed into the possibility of autoimmunity being stimulated by the same viral residue as that responsible and necessary for permanent immunity. Finally, methods of controlling and/or preventing such abnormal response are essential.

The importance of investigating these questions cannot be overemphasized, since the answers will have profound bearing on the understanding and treatment of the post-polio syndrome along with a host of other chronic illnesses such as multiple sclerosis, myasthenia gravis, systemic lupus erythematosus and rheumatoid arthritis.

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Poliomyelitis: Late Pulmonary Complications and Management

D. Armin Fischer, M.D.

Introduction

The last poliomyelitis epidemics in the United States began in the late 1940s and declined dramatically a decade later following the introduction of the Salk vaccine. Cases reported per 100,000 population revealed 37.2 in 1952; this dropped to 17.3 in 1955 and 9.2 in 1956. In 1955 the number of reported cases of poliomyelitis during peak weekly incidents (August to September) was between 2100 and 2400. In 1956 during the same period it had fallen to 900 and in 1957 to 400.[1] The early symptoms of respiratory involvement were associated with increased respiratory effort. Initially this was manifested by increased rate of breathing, dilatation of the nostrils, interruption of speech and use of accessory muscles of respiration. Respiratory paralysis due to involvement of medullary respiratory centers was characterized by irregular breathing and periods of apnea associated with cyanosis and marked anxiety. Analysis of the nature of the respiratory muscle failure in individual patients led to greater understanding of the physiology of respiration and the mechanics of ventilation. Paralysis referable to the cervical cord often involved the diaphragm as well as neck accessories; thoracic cord involvement caused impaired intercostal muscles and impaired abdominal muscles, resulting in a flaccid thorax and loss of effective cough. Patterns of compensation were identified: neck breathers (accessories) who had tolerance limited by fatigue when sitting; in-

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tercostal breathers who retracted abdomen and supraclavicular spaces with breathing; diaphragmatic breathers who breathed well when recumbent associated with expansion of chest and abdomen, but who often needed abdominal support when sitting; and abdominal breathers who had good tolerance when sitting, but lost tolerance rapidly when supine. Modern pulmonary physiology had its beginnings in the confrontation of respiratory polio problems and concerned medical scientists.

Affeldt and colleagues[2] reported functional and vocational recovery in 500 poliomyelitis respirator patients in Los Angeles County who were admitted to the Rancho Los Amigos Hospital for further care and rehabilitation. Their average stay at Rancho was nine months as inpatients. In 1958 follow-up was four to seven years after the onset of their poliomyelitis. Seventy-nine (16%) were dead, 50 (10%) were still using respiratory support and 371 (74%) were reported to be completely free of respirators. Although we do not have complete data on this latter group, it is known that many were left with impaired respiratory reserve and impaired cough.

The present review of Rancho Los Amigos Hospital respiratory outpatients confirms the late return to respirators of many post-polio patients with marginal breathing capacities.

Methods

Charts of 114 polio patients who have been actively followed by the Pulmonary Service at Rancho Los Amigos Hospital for many years were reviewed. All patients meeting that criterion were included. In addition to these patients, 32 people were seen for the first time by the author as a result of increased public awareness and concern following the July 1980 NBC television program "Back to Braces."

Results

Data on the 114 patients are noted in Tables 1 to 3. Nearly all of these patients required respiratory assistance at onset, but many were independent for several years. Of these 114 patients currently followed by the Pulmonary Service at Rancho Los Amigos Hospital, 98 (86%) require some form of assisted ventilation (Table 1).

Table 1. Respiratory Support

Full time	22
Night + daytime prn	70
Day M.P.,* GPB prn†	6
None	16

*Mouth positive pressure
†Glossopharyngeal breathing

One criterion for progression of respiratory disability is a need for tracheostomy. Only 18 (35%) maintained tracheostomies from the onset of their disease (Table 2). Indication for late tracheostomies is given in Table 3. Nearly all of the 36 patients undergoing spinal fusion received tracheostomies at that time. Thirteen retained their trachs because of needed assisted ventilation and/or need for suctioning because of poor cough. Five patients developed late cardiorespiratory failure associated with kyphoscoliosis, a complication probably avoidable if they had received spinal fusion. Five patients developed respiratory failure associated with atelectasis and required tracheostomies. These patients benefited from their trach both as an access for suctioning and for ventilation. The major indication was when previously effective forms of assistance (tank, cuirass, rocking bed, pneumobelt) had become ineffective (26 patients). One patient who required a tank respirator for eight months at the onset of

Table 2. Tracheostomy

Since onset	18
Late post-onset	52
Years after onset	18
	(2-57)

Table 3. Late Tracheostomy Indications

Spinal fusion (36)	13 maintained
Atelectasis	5
Kyphoscoliosis	5
Trauma	2
Progressive ↑ CO2	1
Tank, cuirass, etc.	
Ineffective	26

her polio infection in 1953 developed progressive CO_2 retention in 1978 and required a tracheostomy for respiratory failure. The remaining two patients received tracheostomies associated with acute injury or illness: one with flail upper extremities sustained a subdural hematoma following a fall; the second patient had functioned with a chest cuirass during the night and mouth positive assistance during the day for 30 years, but developed an acute illness, suffered a pneumothorax and cardiopulmonary arrest, was resuscitated, but required a tracheostomy and continuous ventilation subsequently. The late tracheostomies average 18 years post-onset with a range of 2 to 57 years. Of the 16 patients not requiring ventilatory assistance, vital capacities averaged 1700 ml while in the 52 requiring late post-onset trachs, the mean VC was 700 ml (Table 4). The mean loss of vital capacity in ten patients observed for 158 patient-years was 28 cc/year.

Table 4. Vital Capacities

16 Without respirators	1700
	(500-4729)
52 Late trachs	704
	(200-1700)

Of the 32 patients who were evaluated at Rancho Los Amigos Hospital for the first time because of concern for possible complications, the following observations are pertinent. Of the 32 evaluated, 13 were quadriplegics. The others had variable extremity and trunk weakness. One had bulbar symptoms (aspirations plus neck and shoulder residuals). Twenty-two had required respiratory support at onset, and ten required some support at the time of their evaluation. Eighteen had abdominal paresis and ten had some degree of diaphragmatic paresis. Five had tracheostomies, and eight used glossopharyngeal breathing.[3] Vital capacities varied from 100 to 4250 with a mean of 1850. New symptoms were described by only 17. Except for one patient complaining of elbow pain (bursitis), most of the problems were general and nonspecific. Six patients noted increased fatigue, six complained of general weakness, and four complained of dyspnea. One of these patients had documented sleep apnea with O_2 saturation falling to 83%. One patient had nocturnal anxiety symptoms and was found to have inadequate pressures for her

cuirass and decreased O_2 saturation at night. She was given prescriptions for O_2 plus protriptyline at bedtime in addition to correcting the cuirass pressures.

In addition to the two patients noted above, four patients were identified in the group of 114 respiratory post-polio patients who had documented or suspected sleep apnea. One patient began developing symptoms of nocturnal awakening with headaches which were alleviated by deep respirations. The patient used a cuirass at night and was aware of sensations of obstruction in her throat. Nocturnal studies have not been done.

The second patient was obese and used mouth positive pressure six to eight hours at night. He had spirometric studies suggesting upper respiratory airway obstruction, and he was noted to have frequent snoring episodes during sleep and had apneic periods when not on mouth positive respiration.

The third patient was also obese and had significant kyphoscoliosis. He complained of numerous episodes of dyspnea at night without orthopnea. He was referred for sleep studies (1979).

The fourth patient was also kyphoscoliotic and overweight. She was hospitalized with dyspnea, elevated carbon dioxide and hypoxia. Initially she was placed in a Drinker tank. After her recovery from respiratory failure, sleep studies were performed with ear oximetry and capnograph while she was in the tank at night. She showed intermittent desaturation and CO_2 elevation. She was supplied with mouth positive ventilation by a Bennett mouth-seal after nasal C-Pap[4] was not tolerated. Evidence of obstructive apnea was present.

More recently we have acquired a Respitrace[5] which allows simultaneous measurement of chest and abdominal movements. This has enabled us to better document obstructive and central apnea. Two of the above patients were quadriplegic and had VCs less than 1,000. The other two were paraplegic, one of whom also had involvement of the shoulder girdle. It is not clear from the records whether these patients had evidence of bulbar involvement at the time of their acute episode of poliomyelitis. None of the patients were studied at the time we had obtained the Respitrace, so the question of central apnea cannot be resolved in these patients. We found in the fourth patient that the use of mouth positive pressure and protriptyline[6] plus nasal oxygen reversed the hypoxemia at night and appeared to reverse the obstructive problem so the patient was able to sleep through the night.

Discussion

Respiratory problems in 178 outpatient post-polio patients seen by the Pulmonary Service in the past four years at Rancho Los Amigos Hospital have been reviewed. Many of these people experienced late (post-acute) episodes of respiratory failure and became dependent, at least part time, on respirators. Some expressed concern that late functional decompensation in polio patients might represent a new unique syndrome of potentially serious consequences ("Back to Braces," NBC, 1980). The present report deals with late functional respiratory decompensation in polio. The decline in the FEV (28 ml/hr) in the polio group did not exceed that noted in normals.[7] Those patients remaining free of respirators had FEVs that averaged 1 liter greater than the group requiring late tracheostomies. It appears that the loss of tolerance off ventilators can be accounted for as a normal rate of loss in patients with small respiratory reserve rather than by abnormally rapid deterioration of respiratory muscle function. The phenomenon of late respiratory decompensation in other restrictive respiratory disorders is similar: patients with congenital kyphoscoliosis and patients with residuals of extensive tuberculosis, especially with thoracoplasties, are commonly observed to develop respiratory failure late in their course. This supports the hypothesis that normal progression of functional loss can explain respiratory decompensation in these patients with marginal reserve, especially when associated with an acute respiratory complication such as atelectasis, infection or chest trauma.

The syndrome of sleep apnea has been frequently described in recent literature.[8] The usual clinical setting occurs in an obese patient with upper airway obstruction during sleep; however, central sleep apnea is also increasingly recognized. In 1958 Plumb and Swanson[9] described abnormalities in central regulation of respiration in poliomyelitis patients. These syndromes presented primarily as episodic sleep apnea. Guilleminault and Motta[10] reported five patients in 1978 who demonstrated excessive daytime sleepiness and nocturnal episodes of central apnea and often obstructive and mixed apnea. Each of these five patients had experienced polio infections 16 or more years before the onset of symptoms of daytime somnolence. Each of the five patients described had experienced bulbar symptoms during the polio epidemics. Monitoring during sleep revealed "disturbed sleep"

associated with frequent episodes of apnea. Central apnea was predominant (52%), 32% were mixed and 16% obstructive. Hypoxia was associated with the episodes. The authors prescribed night-time cuirass respirators, with symptomatic improvement if frequency setting was eight to ten per minute. In their cases, higher frequencies were noted to cause increase in obstructive apneas. Methylprogesterone did not help. Protriptyline was not tried.

The management of chronic disability requires major patient participation in care decisions. Unlike the patient with acute illness who will recover with appropriate treatment and cease to be a patient, the chronic post-polio patient may be confronted with a new way of life when respiratory failure develops. This change is often strongly resisted by the patients; tracheostomy may be refused despite firm recommendations by the physician. Alternatives may need to be tried until the patient recovers or agrees to the recommendation. Often the patient "puts off" the inevitable trach until the next crisis. This is as it must be. The patient's understanding and consent is, of course, essential. For this group of people who have survived many crises, a change in the nature of respiratory support is a major adjustment. As in all health care situations, compassionate understanding in communication is essential. Some physicians, who should know better, seem uncomfortable dealing with deformity and dependence. They may direct questions to an attendant rather than to the person who is quadriplegic in a wheelchair and breathing by a respirator attached to a tracheostomy,* as if the post-polio patients were not there or incompetent to speak for themselves. The long and often productive survival of severely disabled quadriplegic people who are respirator-dependent and lead active lives in the community is a document to the fierce independence and indomitable spirit of this group of remarkable human beings. Those who disdain the "quality of life" of the "disabled" should observe these people and learn from them. They have much to teach.

*Uncuffed tracheostomies are used in chronic respirator-dependent patients so they may speak. The respirator volume may need to be increased to provide adequate ventilation.

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Orthopedic Management of Post-Polio Sequelae

Jacquelin Perry, M.D.

Introduction

Poliomyelitis creates a unique lesion. By selectively attacking the anterior horn cells within the spinal cord, the virus causes structural muscle weakness, but leaves all sensation and motor control intact. As a result, patients have a reduced ability to perform normally but unlimited capacity to substitute.[1] This is the basis of their current dilemma.

Today many adults who had poliomyelitis 30 plus years ago are experiencing pain and increasing muscle weakness. Among 193 persons seen in the Rancho Polio Clinic these incidences were 62% and 33%, respectively. The causes of pain are postural substitution for weak musculature, fixed deformities and muscle overuse. Mechanical strain is the common denominator. Excessive knee hyperextension (48%) and lordosis (15%) are the most frequent postural substitutions. Knee valgus, ankle equinus and scoliosis are the common deformities. Sites of increasing weakness occur in both upper and lower extremity musculature.

The most common problems will be described in detail. An explanation of the causative mechanisms will provide a basis for extending these examples to the other sites of impairment.

Knee Hyperextension

Patients who lack adequate quadriceps strength use hyperextension to lock their knee for weight bearing stability (Fig. 1).

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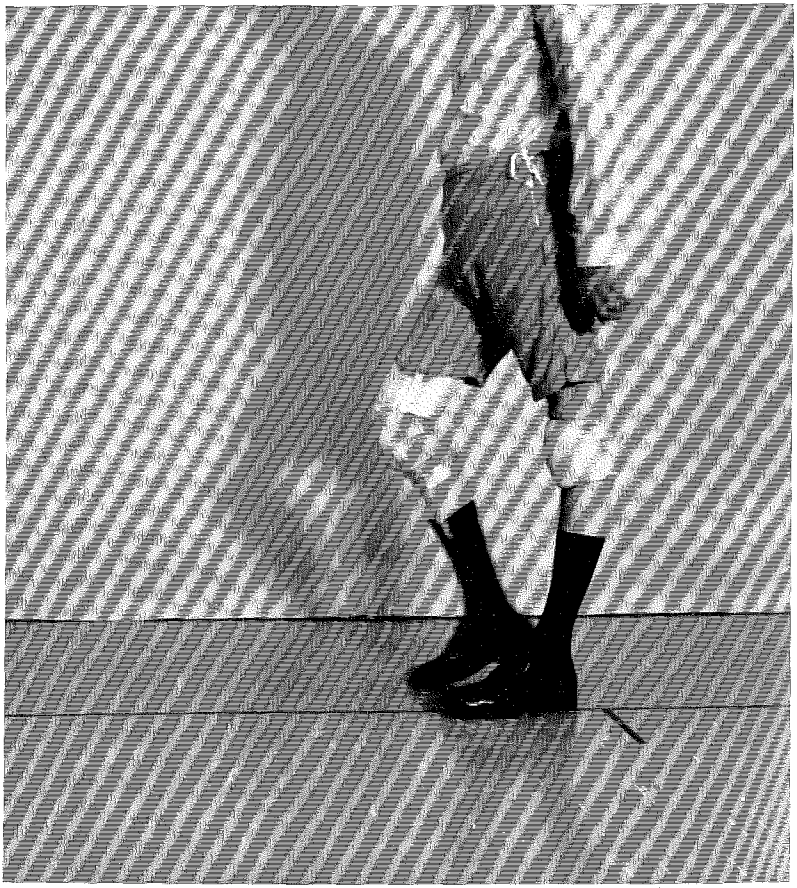

FIG. 1. 20 years post-polio (1973). Genu recurvatum substituting for the poor (Grade 2) quadriceps and calf muscles to provide knee stability for weight bearing. The three pads are for protection against periodic falls when postural stability has not been gained in time.

This presents two potential problems: loss of normal shock absorption mechanisms and increased strain.

Normally, joint stress during limb loading is avoided by two shock absorbing actions. Floor contact with the heel initiates a rocker action which rolls the foot into plantar flexion and draws the tibia forward to flex the knee.[2] The extensor leverage present at the onset of stance is reversed into a flexor torque. This

transfers much of the loading force to the quadriceps mass. It also releases tension on the ligaments. Additional protection is provided by the hamstring muscles. During mid-stance the calf muscles actively stabilize the tibia so the quadriceps can initiate knee extension.[1] As body weight moves forward of the supporting foot in terminal stance, the knee approaches extension (0-5 °flexion). Again, hyperextension is avoided by muscle action and the creation of flexor torque. Throughout terminal stance vigorous contraction of the gastrocenemius muscle provides posterior protection. Then at the end of this phase rapid knee flexion is initiated by the tibial falling forward over the forefoot rocker. As a result, stress on the ligaments is brief and of low magnitude.

The knee gradually extending from a flexed position throughout stance also contributes to joint cartilage health. By continually changing the weight bearing area, there are no points of concentrated stress.

When knee hyperextension is used to substitute for a weak quadriceps, body weight is aligned to create a passive extensor torque (Fig. 2). Posterior stability is provided by the joint capsule and ligaments. As long as this alignment can be maintained, knee stability is good. Hence, patients assume this posture with initial floor contact and hold it throughout stance. As a result, the posterior ligaments are asked to accept an unusual force and it is sustained for at least a full second with each step since such polio patients walk at about half normal speed. During this period body weight is concentrated on one area of joint cartilage.

The amount of strain experienced is proportional to the knee joint angle (Fig. 3). This, in turn, is influenced by the strength of the hip extensors and ankle plantar flexors. When these muscles are strong, minimal forward alignment of body weight is sufficient to stabilize the knee. Even a 15° flexion contracture can be accommodated. Also, the hamstrings and gastrocnemius provide active support. Hence, patients dependent upon gross knee recurvatum are evidencing significant paresis of the extensor muscles at all three joints. The final limb posture represents substitution for all three areas of weakness (backward trunk lean, knee hyperextension and ankle plantar flexion).

Clinical experience indicates that knees which hyperextend no more than 10° can have passive stability without a signifi-

FIG. 2. 31 years post-polio (1984). Knee deformity has increased with a subsequent 11 years of depending upon genu recurvatum for knee stability. Vertical white line is a visual display of the body weight vector recorded by the force plate. Distance between vector and knee joint center (circular marker) identifies the moment arm which is directing body weight into a deforming force (creating posterior ligament ligamentous strain).

cant strain. Ranges of 20° or more are susceptible to progressive damage. Moderate genu recurvatum is a common inherited trait which may place the adult polio patient in jeopardy. Childhood growth responses to walking in hyperextension lead to more severe molding of the joint surfaces and ligaments.

Several factors contribute to deformity progression. Tension reduces tissue vascularity leading to microdegeneration.[3] Chronic strain causes polymer lengthening (creep) of the collagen fibers.[4] Repeated tension would result in longer fibers with collagen turnover (half-life 300 days).[5] Theoretical calculations indicate the ligamentous strain with a 10° knee angle would be approximately 40% of the average failure level for an acute injury.[6] This increases to 76% with a 20° deformity, sufficient to cause individual fiber rupture, as subtle differences in alignment vary their exposure to the imposed forces. As fibers are lost, ligament strength is reduced and lengthening increased. Theoretically, a 30° recurvatum leads to forces that exceed the failure level. Similar forces are being imposed on the weight bear-

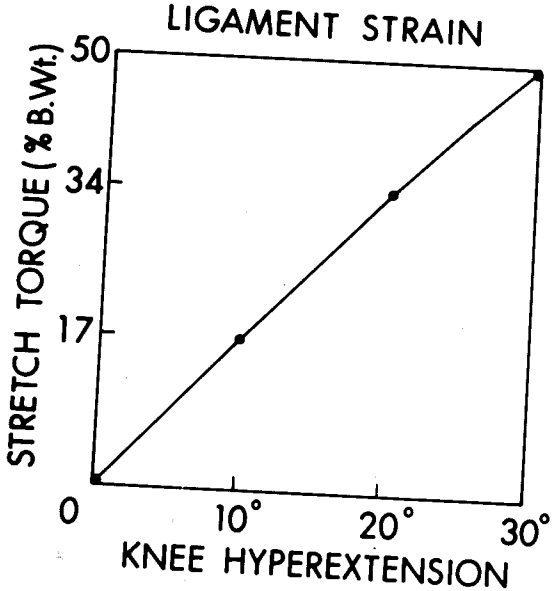

FIG. 3. Ratio of ligamentous strain in the hyperextended position at the knee.

ing area of joint cartilage. Repeated excessive impact has been shown to cause joint degeneration.[7]

These many factors govern the clinical programs designed to relieve pain while maintaining the patient's ability to walk. The therapeutic challenge is to preserve the patient's free knee flexion for swing, retain sufficient hyperextension for weight bearing stability, yet reduce the deformity to a pain-free angle. There are both orthotic and surgical answers.

Supporting the knee with an orthosis requires careful alignment and close fitting. A full length knee-ankle-foot orthosis (KAFO) with a hyperextension knee joint is needed (Fig. 4). For adequate leverage the thigh cuff should be within two finger-breadths (3 cm) of the ischium.[8] The hyperextension knee joint sets the hinge about 3 cm behind the axis of the uprights. This allows the orthosis to lock before the anatomical knee completes its extension. As a result, knee ligament strain is reduced. One must avoid the standard brace joints which actually are set in about 15° flexion. Under ideal circumstances the orthosis is aligned to place the patient's knee in only 10° hyperextension, but generally an angle closer to 20° is needed to provide an adequate sense of stability. The orthotic ankle joint must allow sufficient plantar flexion for flat foot floor contact so all heel rocker action is avoided. Stability in terminal stance is improved by use of a 5° dorsiflexion stop.[9] This can be combined with a dorsiflexion assist when the pretibial muscles are weak. Patients have to accept a slightly shortened step in exchange for the added stability. Also, double channel joints and stronger stirrup are needed. Both add weight to the orthosis. A well-fitted orthosis using aluminum uprights and free ankle joints weighs about 3 pounds. Since hip flexor muscle weakness commonly accompanies quadriceps paralysis, this is a significant factor.[10] The patient's orthotic tolerance can be judged by having the patient attempt hip flexion with a 3 pound weight at the ankle. Raising the limb 20° or 30° is sufficient during walking.

Surgically one can reinforce the posterior structures of the knee with a triple tenodesis.[11] This is a procedure I designed in 1968 to correct the severe deformities that develop during childhood when early protective bracing was not provided. The

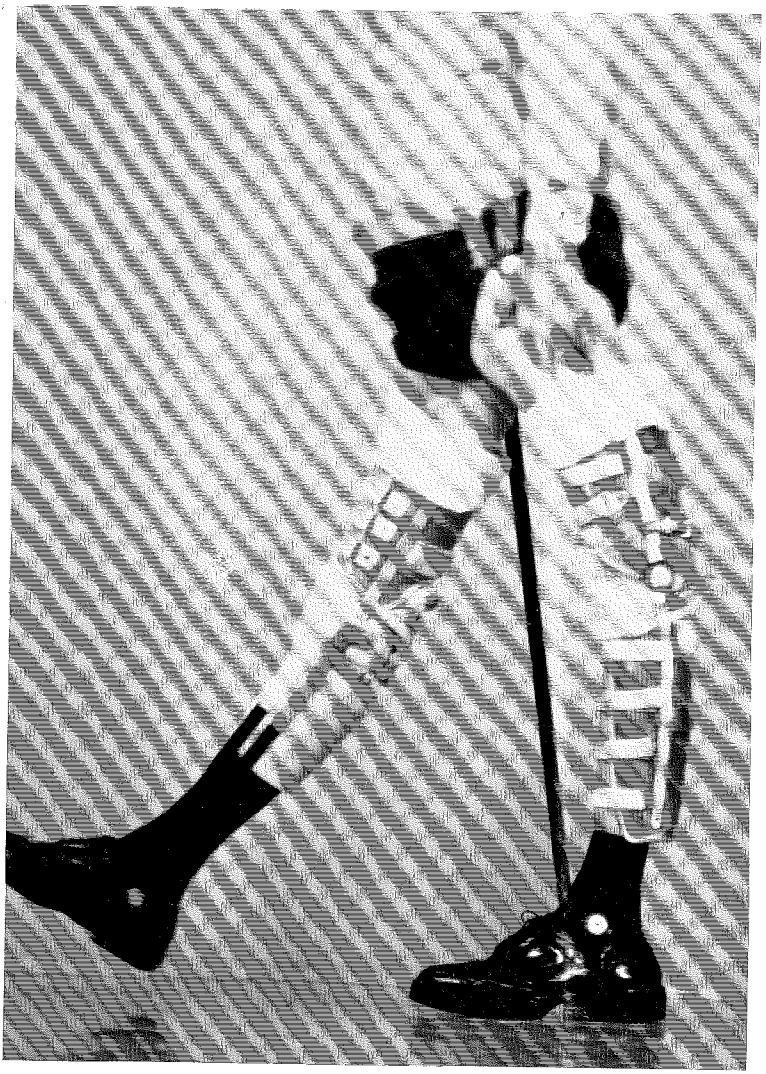

FIG. 4. Reduction of the genu recurvatum by a knee cap on left and a full knee orthosis on right. Compare stability of tibial segments of the two orthoses and also note simple joint on knee cage and hyperextended joint on right orthosis to provide an earlier postural lock.

rationale is to create a mass of connective tissue sufficient to accept the forces of moderate hyperextension. For this purpose a central restraining ligament between femur and tibia is fashioned from the tendons of the gracilis and semitendinosus. Reinforcing diagonals are constructed with the anterior half of the iliotibial band and biceps femoris tendon. These structures are supplemented with the tendons of the semimembranosus and lateral head of the gastrocnemius, respectively. Initial experience with the procedure was with teenagers in Hong Kong. It has been applied to only a few American adults. Success in the latter group has varied with the quality of the patient's tendons and willingness to wear a protective orthosis for a year (J. Stuart Gaul, personal communication). This is a critical factor since adequate strength at the suture lines can be gained only through connective tissue maturation, and this is a slow process. Shortcutting this step leads to recurrence of the deformity. Very possibly artificial ligaments will lessen both problems. Tissue insufficiency would be supplemented and internal splinting could shorten the need for orthotic protection. Correction of any existing ankle equinus or the use of an orthosis to supplement plantar flexor weakness also are essential. There can be no added demands placed on the knee.

Knee Valgus

Similar types of stress are placed on the ligaments and joint surface. The cause is dependence on a Trendelenburg limp to accommodate weak hip abductors. Ligamentous instability which allows neutral alignment is readily controlled with a KAFO. Stability is better gained with a molded anterior, lateral tibial shell than a medial condyle pad since a broader contact area is supplied. Rigid deformities greater than 15° are difficult to support, however, since the lateral trunk shift creates a strong deforming torque. Stainless steel uprights, often with reinforcements, are needed.

Surgical correction of a rigid deformity by osteotomy is indicated when bracing is no longer effective. It also is an alternate to indefinite dependence upon an orthosis. To maintain the correction during the bone maturation period a KAFO is needed for one year. Otherwise, the new bone will yield to the still present deforming force used to stabilize the paretic hip. At present there are no surgical answers to medical ligamentous instability.

Lordosis is the second most common adult polio problem seen in my clinic. Use of back hyperextension to substitute for paralyzed hip extensor muscles is the primary cause.[1] Hip flexion contractures accentuate the problem since a greater degree of lordosis is needed to gain passive hip stability. Pain results from the body weight line being transferred from the vertebral bodies to the lumbosacral facets (Fig. 5). Neither their size nor vertical alignment is appropriate for this task. High sheer forces result with secondary degenerative changes. Generally these are not apparent by x-ray. Clinical answers are difficult for the ambulatory person. Crutches to assume part of body weight and to reduce the dependence on lordosis for hip stability are the best

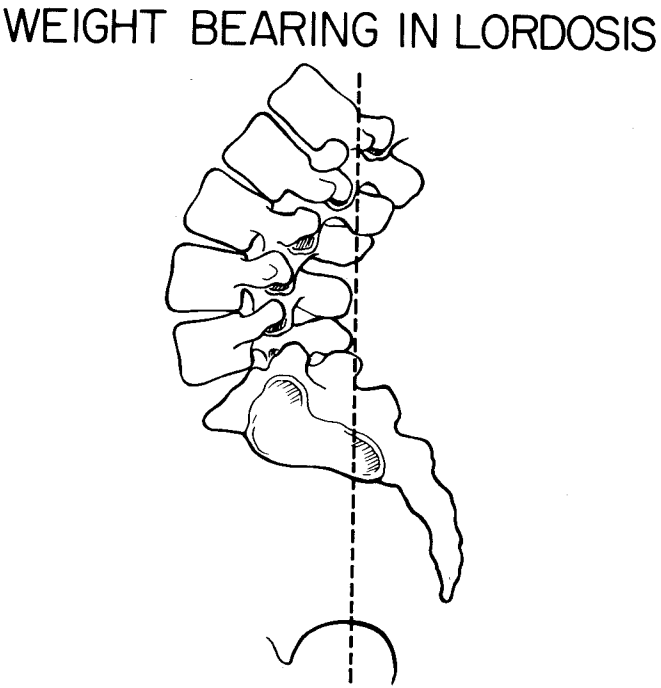

FIG. 5. Body alignment with weight bearing lordosis. *Dotted line:* Body vector between trunk mass and hip joint. Distance between vector and facet joints is proportional to the extensor torque body weight is creating on those joints. This is an indication of the strain joints are experiencing.

solution but a difficult one for patients to accept. A corset provides a useful hyperextension restraint for some people.

Degenerative Arthritis

Chronic weight bearing on any deformed joint causes stress concentrations which often lead to pain.[12] Total joint replacement must be approached cautiously, since paretic muscles provide insufficient protection from the passive forces of walking. Orthotic support or joint fusions are more reliable answers.

Spine deformities which become painful are a particular problem. Surgical stabilization is a major undertaking for adults. Severe deformity and the presence of muscle paresis reduce the probability of successful stabilization.[13] Hence, a corset or a molded jacket is indicated. Modern plastics allow excellent molding, are light, easy to clean and not bulky.

Muscle Weakness

Post-polio recovery of muscle strength, as identified by manual testing, creates three functional classes: Good to Normal (grades 4 and 5), Poor to Fair (grades 2 and 3) and Zero to Trace (grades 0 to 1). Patients with "Good to Normal" muscles have the physical capability to function in a normal manner. As a result, it was assumed that these manual grade differences were insignificant, i.e., 4/5 vs 5/5. Beasley's quantitated measurement of patients' manual muscle test values and their comparison to the strength of normal persons of similar age presented a different picture.[14] He found grade Good (4) strength was only 40% of true normal (Fig. 3). Also, a post-polio Normal averaged 75% of true normal. The low value for the Good grade is substantiated by Sharrad's postmortem findings that muscle weakness was identified by clinical testing only when more than half of that muscle's anterior horn cells had been destroyed.[15] These findings mean that the muscles with Good strength must work 2½ times as hard (40 vs 100 motors) as does normal musculature.

Ability is extended by subtle substitutions which transfer some of this demand to stronger muscles or the ligaments. Thus, initially, musculature with Good and Normal minus strength differs from those which are truly normal only in the exertion required for each activity.

Patients with Fair and Poor strength rely more heavily on substitution. They mix passive ligamentous stability with brief periods of active control so the total demand is within an acceptable range. Many of these patients started with orthoses and then gradually found ways to get by without them. Again, the remaining muscle fibers have to contract for longer than normal periods.

Clinical experience is now telling us this type of strenuous use can be tolerated about 30 years. Then there is no further reserve and a functional loss is experienced. If the overuse is caught quickly and the patient's habits changed to a physiologically acceptable level, the lost strength can be recovered. One example is replacing a manual wheelchair with an electric model to save severely paretic arms.

The therapeutic program, hence, is avoiding overuse by life style modulation. Assistive devices, orthoses and functional training for more effective use of the remaining normal musculature are the technics. Strengthening exercises are not appropriate unless one is focusing just on the noninvolved muscles. The basic problem is overuse of paretic muscles rather than disuse. Convincing patients often is difficult, however. Such people are provided a carefully designed exercise program and explicit cautions that persistent fatigue or greater weakness following the exercises indicates overuse and the program should be stopped. Patient experience has confirmed this assumption and that other measures are indicated. When the prescription of assistive orthoses is not indicated, more subtle forms of life style redesign are required. This necessitates clever planning by very knowledgeable occupational and physical therapists.

Upper extremity strength can be easily overestimated because it varies so markedly throughout the range. Elbow flexors which are graded Good at 90° will be Poor when the arm approaches the full extended position. Hence, reaching is a strain. The shoulders present a reverse picture with greater strength being in the low ranges of elevation (0-45°).[16] Hence, a person may be functionally competent for those activities which can be performed with the elbow flexed and the arm at the side. Wheeling a chair requires a greater arc as do many household tasks.

In the lower extremity calf muscle weakness is a subtle but critical cause of reduced function. The soleus and gastrocnemius stabilize the tibia so the quadriceps must work harder (unless one

has knee hyperextension). Two functional patterns are seen: avoidance of all knee flexion in stance or persistence of the flexed knee posture. Both represent excessive quadriceps use and causes of fatigue. By early intense action the quadriceps can prevent knee flexion during limb loading. This lessens the effort required to maintain knee extension over a tibia that does not have a stable base (ankle control lacking). Patients with a slight flexion contracture or dependence on the hamstring to assist the gluteus maximus have a flexed knee during the entire weight bearing period. Quadriceps demand is high and endurance correspondingly reduced. The therapeutic answer is a dorsiflexion stop orthosis. Double channel, adjustable ankle joints are needed. Rods in the anterior channel provide a positive limit. Adjustability is needed to allow optimum alignment. The difference between 5° dorsiflexion and neutral seems small, but it can have a major impact on the person's ability to walk. Springs are futile since adequate force is not possible. Use of the posterior channel varies with need. Leaving it open allows ankle plantar flexion for a normal loading response. The addition of a dorsiflexion spring provides toe pick-up in swing. Plastic orthoses are not appropriate because they cannot combine stability and mobility. The surgical equivalent is an ankle fusion with the joint at neutral. This provides the needed dorsiflexion stop for efficient quadriceps function. Tarsal joint mobility allows the limb to appropriately advance over the supporting foot. The subtalar joint offers 15° plantar flexion for a normal loading response, while the mid-tarsal joints yield 5° dorsiflexion to advance body weight onto the forefoot for an appropriate terminal stance.

Perspective

None of these problems are new. They merely are unexpected, having occurred in an adult population that substituted very effectively for many years. Also, most of these patients had good early care which minimized their deformities. Hence, the development of complications occurred late.

In the acute polio patient with very uneven involvement, local overuse of a muscle group was not a rare finding. The secondary loss of strength could be fully recovered with prompt protection by an assistive orthosis. Conversely, persistence in the straining activity resulted in permanent loss. Excessive hyperex-

tension of the knee and valgus as well as other deformities still are common in children who do not receive good early management. This is the group which stimulated the triple tenodesis procedure and most osteotomy surgery.

The one significant difference is the development of pain. In adults the absence of growth concentrates the forces in the mature tissues. Degenerative change rather than tissue remolding is the consequence.

One of the major deterrents to therapeutic effectiveness is the patient's failure to recognize the extent of change that is needed. They have "gotten by" so well for so many years it now is hard to appreciate that they were exhausting a functional reserve which now must be replaced with a major change. Recognizing their symptoms as evidence of chronic strain provides a rationale for both therapeutic design and patient acceptance.

The new challenge is to design optimum protective programs for the patients who are just beginning to experience functional loss. Responses should be prompt. Wishful thinking that the problem is temporary is detrimental.

Summary

The underlying factor is chronic mechanical strain which has used up the tissue reserves in the ligaments, joint surfaces and/or muscles. Orthopedic management is directed toward preserving function by relieving the strain. The therapeutic measures are orthoses, reconstructive surgery and life style modifications.

The current problems, really, are a credit to how well polio patients can substitute. These lessons need translation into protective programs for patients just beginning to experience a reduction in function.

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Polio Residuals Clinic and Exercise Protocol: Research Implications

Richard R. Owen, M.D.

Introduction

We have established a polio clinic at Sister Kenny Institute to respond to expressed concerns of former polio patients and to serve as a component of research to determine the extent and nature of the late effects of paralytic poliomyelitis. The Sister Kenny Institute was founded in 1942 to serve as a regional center for the management of acute poliomyelitis. The medical staff has had a continuing interest in the problems associated with poliomyelitis. Orthotic review and periodic reassessment of polio patients has been an outpatient clinic function. Sporadic acute cases have been treated at Sister Kenny since 1960. Although individuals were occasionally seen with problems of progressive weakness and disability, a major resurgence of interest has occurred in the last three years.

The First International Conference on Respiratory Rehabilitation and Post-Polio Aging Problems was held in Chicago in October 1981. The scientific and emotional impact of that conference is well described by Raymond and Laurie.[1] We held our first conference at Sister Kenny Institute in February 1982 and have held two additional conferences since then. Conference participants were surveyed with regard to progression of weakness and disability. They were also asked about their activity and exercise levels. I developed an exercise protocol based on the survey results and the clinical assessment of patients seen in our outpatient department prior to the establishment of our

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Respiratory status at the time of acute infection and now is established by record review and history. As I indicated earlier, we have not seen the expected incidence of ventilator-dependent individuals in our clinic and at our conferences. Our survey data indicate that 40% of the respondents experienced unexplained pain. In the 126 individuals seen in our clinic, the pain syndromes appeared to be commonly associated with musculoligamentous injury, mechanical skeletal stress or deconditioning. Hypochondriasis and neurosis were less commonly associated factors. Those individuals with pain also experienced various degrees of intense fatigue. Our patients participating in a regular conditioning exercise program often report a gratifying relief of pain and fatigue. Vallbona and Baker have recently reviewed physical fitness as it relates to the elderly and disabled.[5] Overuse abuse and the insensitivity to fatigue in former polio patients have been issues of concern and have been well studied and reported on by Bennett and co-workers at Warm Springs.[6,7] We have had two patients comparable to the four reported by Bennett.[6] One of our patients responded to a gently graded exercise program of progressive resistive exercises and conditioning. A number of patients reported temporary weakness after injudicious exercise or activity. Strength returned after a rest period.

I have seen one former polio patient who later developed multiple sclerosis. I have seen no individuals with amyotrophic lateral sclerosis superimposed on poliomyelitis residuals. In our polio clinic group, we have had two individuals with cerebral palsy, two as yet undiagnosed individuals with upper motor neuron disease and one with childhood hemiplegia, all mislabeled as polio. Many of our patients had been extensively studied elsewhere for neurologic disease with electromyography, spinal taps, myelography and tomography. In many instances the progression of weakness was so insidious that the patient noted the change retrospectively based on need for additional ambulatory aids. Fracture of an involved extremity and various musculoligamentous injuries have resulted in substantial loss of function. Defining the degree of pre-injury disability has been a complicating issue in personal injury and workers' compensation cases. Forty-eight percent of 145 respondents at our second and third conferences indicated additional weakness in response to exposure to cold. Dr. Herbison has suggested that I study the

Polio Clinic. Our survey considered the following: (1) progression of weakness, (2) unexplained pain, (3) deconditioning, (4) additional neurologic disease, (5) additional musculoskeletal disability and (6) effect of cold. The conferees were individuals who had concerns about the late effects of poliomyelitis and therefore represent a select group of respondents. Only three of the attendees at our conferences were presently using ventilators. Only one ventilator-dependent patient has been seen in our clinic. This important group may be experiencing another variety of problems. Dr. Knapp will study former polio patients treated by the medical staff of the Institute during the epidemic year of 1952. We hope to learn the status of ventilator-dependent individuals as well as determine the number of former patients untroubled by the late onset of additional disability.[2]

Survey Results

One hundred eighty-eight individuals with polio residuals responded to the survey at the first three Kenny polio conferences. Eighty percent indicated that they had experienced significant progression of weakness. Forty-three percent required additional mobility aids. Fifty percent indicated that they experienced pain in the neck and shoulders. Despite mechanical factors that would seem to predispose to herniated disc disease in the cervical and lumbar spine, 1% (2 of 188) had cervical disc surgery and 3% (6 of 188) had low back surgery for disc disease. Eighty percent had cold feet and 48% had additional weakness on prolonged exposure to cold. Although a number of the conferees had been evaluated for amyotrophic lateral sclerosis, none were found to have that disease. The relationship of poliomyelitis to amyotrophic lateral sclerosis was reviewed by Mulder in 1972.[3] One respondent now has multiple sclerosis. One individual was told that she had a latent polio virus, but this was not confirmed by virus studies. I prepared a paper summarizing the nature of the problem, the survey data and the basis of the exercise protocol to provide information for the clinic and conference participants.[4]

Clinic Purpose

A major purpose of the clinic is to define the nature of the multiple and interacting origins of the progression of disability

long after acute poliomyelitis. It is important to establish the incidence of disability progression based on simple and explainable biomechanical factors. The following factors are considered in the clinical assessment: (1) the loss of marginal muscle function with aging and related loss of mechanical balance, (2) undertraining effect associated with decreased exercising, (3) overuse abuse of weakened muscles, (4) cardiopulmonary deconditioning, (5) prolonged musculoskeletal stress, (6) intercurrent health problem, (7) newly superimposed neurologic pathology and (8) miscellaneous psychosocial factors.

Clinical Assessment

The clinical protocol is defined in Table 1. The history of additional disability includes age and date of onset of polio and date of onset of the progression of disability. Most patients date the onset of additional disability 25 to 30 years after acute polio.

Table 1. Clinical Data - History

Clinical data
Patient survey
Record review
History
1. Date and age of onset
2. Progression of weakness
3. Respiratory status
4. Experience of pain
5. Experience of fatigue
6. Overwork effect
7. Additional neurologic diagnosis
8. Additional ambulatory assist
9. Musculoskeletal injury
10. Degenerative arthritis
11. Disk disease
12. Effect of cold
13. Sleep disturbance
14. Mobility and activity
15. Exercise level
16. Cardiopulmonary conditioning
17. Weight gain
18. Smoking history
19. Change in life style
20. Psychosocial vocational issues

effect of cold on post-polio patients (personal communication, 1983).[8] It would be valuable to investigate the problem and to determine the impact of conditioning programs and muscle training on that type of weakness.

Activity level and physical hygiene issues are addressed. A high incidence of suspicion should be maintained for sleep disturbances, particularly for those individuals who had had bulbar or high spinal poliomyelitis. The Sleep Research Laboratory at the Hennepin County Medical Center has studied two of my patients. The medical staff indicated that they had seen other individuals with polio residuals presenting with fatigue, attention difficulties and sleep disturbance (M. Mawhoud, personal communication, 1984). Many of the patients seen in our clinic indicate that their physical mobility and activity levels may have been reduced even prior to the sense of progression of weakness. The question of which came first arises from the standpoint of reduced opportunity to exercise and train. I have been involved in wheelchair athletics for ten years as a participant and as an examiner, and I have had no active post-polio wheelchair athletes express concern about progression of weakness, easy fatigability or unexplained intense pain. A number have cut back on walking in favor of wheelchair ambulation by choice. None of the subjects at our conferences or in our clinic had been on a regular cardiopulmonary conditioning program.

Weight gain and obesity were not extraordinarily prevalent in the groups surveyed and seen in the clinic. The additional disabling effect of obesity can be a critical functional issue.

The emotional impact of progressive disability associated with aging is obvious. This is superimposed on the psychosocial and vocational problems facing middle-aged persons. We have seen five individuals in our clinic seeking early retirement or long-term disability benefits. Disability determination under Social Security should be addressed as a special problem facing the more severely disabled but presently employed former polio patients.

Physical Assessment

The physical assessment is outlined in Table 2. Isokinetic muscle strength is measured on the Cybex II (M. Mawhoud, personal communication, 1984). We do not have a gait analysis lab.

Table 2. Physical Status Assessment

Physical assessment
Gait
Range of motion
Muscle strength
1. Manual muscle test
2. Trunk strength
3. Cybex II
Neurologic examination
Additional studies
1. Electromyography
2. Neuroradiology
3. Stress test
4. Psychometrics
5. Sleep apnea lab

It would be very interesting to do energy studies on our patients while walking. The benefit from ambulatory aids, orthotics or perhaps wheelchair ambulation could be better defined for our patients. Range of motion, manual muscle testing and neurologic examination are done in the traditional fashion. Special diagnostic studies have often been done prior to our clinic to pursue the cause of progressive weakness, easy fatigability, pain or respiratory distress. Formal stress testing is done in individuals who are at risk in starting an exercise program. Occasionally, cardiologic consultation is required. If sleep apnea or sleep disturbance is suspected, the patient will have sleep studies.

Exercise Protocol

Our exercise protocol is well defined and is explained to the patient in detail as defined in Table 3. The stretching program is primarily directed to hip flexors, anterior thigh musculature, hamstrings and calf musculature. Tight hamstrings and calf musculature were common causes of deteriorating ambulation and/or orthotic problems.

Trunk mobilizing exercises, particularly carried out in conjunction with straight and oblique abdominal strengthening,

Table 3. Exercise Protocol

Exercise protocol

Stretching
1. Prolonged stretching (calf)
2. Flexibility exercises (hamstring musculature)
3. Mobility (trunk)

Trunk strengthening
1. Reverse sit-ups
2. Back extension
3. Trunk isometrics

Resistance exercises
1. Cybex measurements
2. Isokinetic exercises
3. Resistive exercises (home program)

Muscle reeducation
1. Kenny techniques
2. Facilitation (trunk and proximal muscles)
3. Functional electric stimulation
4. EMG biofeedback
5. Powderboard
6. Pool exercises

Gait training

Cardiopulmonary conditioning
1. Exercise bike
2. Arm ergometer
3. Wheelchair roller
4. Therapeutic pool

proved beneficial in those patients presenting with mechanical back disorders superimposed on the preexisting polio residuals. Reverse sit-ups are particularly useful in the presence of hip flexor weakness and/or less than antigravity trunk flexors.

Resistive exercises are initially carried out on the Cybex II. We are able to establish baseline strength measurements, strength decrement curves and relative deficits.[9] The quadriceps and hamstring musculature and the calf musculature are chosen in the lower extremities and the biceps and triceps are chosen for upper extremities when the weakened musculature can be compared with the opposite side. The test results are used to develop

the home exercise program and add incentive for compliance with the program. Isokinetic exercise apparatuses are available in many communities. Home resistive exercises are set up within the framework of the patient's capability and resources. We have had no instances of "overwork" weakness in response to the rigorous testing. Those individuals who have returned for their three-month interval follow-up have demonstrated improvement in the fashion described by DeLorme.[10] He concluded that rapid initial improvement noted in his patients must be related to motor learning.

Muscle reeducation in individuals with poliomyelitis could best be considered in the light of Sister Kenny's term "mental alienation."[11] I believe that the loss of function in muscles working at less than an antigravity grade represents an undertraining or detraining effect. We have used a variety of techniques including the Kenny method, facilitation, functional electric stimulation, biofeedback, powderboard exercises, and pool therapy. The patient frequently notices renewed awareness of muscle contraction in the early treatment sessions. If that contraction has no particular functional implication, it is probable that the quality and force of the muscle contraction will decay unless the patient makes an effort to maintain it. The use of electric stimulation is only for purposes of muscle reeducation of muscles previously functioning and not for "strengthening."[12] The use of the powderboard or therapeutic pool for gravity-eliminated exercises in conjunction with muscle reeducation can further enhance awareness of muscle function.

Cardiopulmonary conditioning may be the most important component of our exercise program. In our follow-up clinics, compliance with a conditioning program is as common as with muscle training. The value of and the associated problems with fitness programs for handicapped individuals have been reviewed by Harpuder[13] and Vallbona.[5] An exercise bike with a flywheel driven by arms and/or legs has proven to be most useful in individuals with scattered residual paralysis. Arm ergometers and wheelchair rollers are most useful for paraplegic polio patients. High technology lightweight wheelchairs make a variety of conditioning opportunities available to those who might be interested in wheelchair athletics. Swimming remains a mainstay of aerobic conditioning. The key to compliance in a conditioning

program is agreed upon objectives and goals within the framework of the disability.[14]

Additional Interventions

Additional interventions include evaluation for assistive devices and for psychosocial services as indicated in Table 4. The evaluation and gait analysis may indicate the need for additional ambulatory assist. Inefficient energetics in ambulation may contribute to the late onset of additional disability in these patients. Many patients have need for multiple options for ambulation. While no assist may be needed for household ambulation, two sticks may be necessary for community ambulation, and a wheelchair may be required for distances and conditioning. Adaptive equipment for improved efficiency, comfort and safety is offered. The clinic patients are presented with information about orthotic developments. Many patients were wearing their original bracing or patched-up versions of that. Lightweight plastic orthotics with better knee and ankle control offer a more energy-efficient gait.

Education and counseling are critical components in the management of progressive disability. The patients receive copies of their medical evaluation, physical therapy assessment, exercise physiology workup and home program. Feedback after follow-up visits also serves as an incentive by providing the individual with a sense of responsibility and a sense of option. Referral to therapeutic recreational programs is made whenever

Table 4. Additional Interventions

Assistive devices	
	Ambulatory aids
	Wheelchair
	Orthotics
	Adaptive equipment
Psychosocial interventions	
	Therapeutic recreation
	Psychologic counseling
	Vocational rehabilitation
	Social services

available. Psychologic assessment and counseling are often prescribed when intercurrent mental health problems exacerbate the post-polio late effects or interfere with compliance in an exercise program.

Vocational rehabilitation and social service assistance are needed for those individuals who are facing critical vocational and life change decisions. As indicated earlier, these issues are often the major presenting problem at the time of referral to our clinic. There is a need to develop sufficient information about the "post-polio syndrome" to help this group in preparation for disability determination by the Social Security Administration or by insurance companies.

Polio Clinic Follow-Up

The follow-up schedule is set after the individual exercise protocol is developed. The nature of the follow-up protocol is shown in Table 5. Physical therapy review sessions are scheduled monthly for two months. The therapist rechecks the manual muscle test, gait and isokinetic strength. The exercise program is reviewed and revised. Exercise compliance has been high for the group participating in the program. None have experienced overuse abuse despite resistive exercises. Conditioning has been beneficial in those individuals troubled by pain and fatigue. Progressive resistive or isokinetic exercises produced an increase in strength, particularly in the quadriceps musculature. This confirms earlier work by DeLorme[10] and Muller.[15] Muller concluded that continued intentional training is necessary to maintain strength in partially paralyzed muscles. Reduced effort lowers the stimulus to maintain strength and allows it to fall to the level of the reduced demands.[15] This would help explain the quick responses of underutilized marginal muscles to a variety of reeducation techniques.

The patient is seen in the clinic at the time of the third monthly physical therapy reassessment. The physiatrist obtains an interim history including comfort level, exercise compliance, overwork effect, subjective change, pain and fatigue status and intercurrent health issues. The physical evaluation is repeated. The exercise physiologist reevaluates the patient who has been previously seen for consultation and stress test. The staff members present oral reports to the patient. The patient receives a copy

Table 5. Follow-up Protocol

Follow-up at one- and two-month intervals
- Physical therapy review
  1. Manual muscle test
  2. Cybex II
  3. Conditioning review
  4. Revise home program
  5. Gait assessment

Polio clinic follow-up
- Physical therapy review
- Interim history
  1. Comfort level
  2. Exercise compliance
  3. Overwork effect
  4. Subjective improvement
  5. Pain and fatigue effect
  6. Intercurrent health issues
- Physical evaluation
  1. Range of motion
  2. Review strength status
  3. Assess trunk strength
  4. Gait
  5. Neurologic status
- Exercise physiology
  1. Review cardiopulmonary status
  2. Repeat stress test
- Patient review
  1. Oral and written report to patient
  2. Counsel patient
  3. Establish follow-up date

of the follow-up clinic data. Further clinic appointments are established as indicated. Our formal protocol extends to the three-month recheck. This group of individuals will help us better understand the origins of the late effects of polio.

Summary

I have reported on the development of a post-polio clinic and an exercise protocol at Sister Kenny Institute. One hundred eighty-eight former polio patients attended conferences held at the Institute. One hundred twenty-six individuals with polio residuals have been seen in our clinic to this point. The multiple

and interacting origins of the progression of disability are considered in the evaluation. We have developed an exercise protocol for purposes of stretching, mobilizing, trunk strengthening, resistance exercises, muscle reeducation, gait training and conditioning. There has been excellent compliance with the exercise program. All the participants feel better. This may be related to the increase in physical activity. Most participants enjoy an adapted conditioning exercise program. The initial return of muscle contraction and the rapid increase in strength in non- or low-functioning musculature in response to muscle training is consistent with the work of both DeLorme and Muller[10,15] Contractures were often associated with gait deterioration. The incidence of progression of disability will be further studied by following our present group of patients, surveying wheelchair athletes and studying the Kenny patients from the epidemic year of 1952.

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Summary of Reports*

Development of Clinical Evaluation Protocol

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Objectives

1. To identify the information necessary to define the clinical problems patients face;
2. To establish uniform guidelines for clinicians in collecting comparable data at various rehabilitation centers;
3. To develop guidelines for follow-up such as the key parameters that will be retested;
4. To outline factors within the clinical setting that will guide and supplement research efforts;
5. To use available basic research information to enhance the success of clinical efforts.

An interdisciplinary clinic provides the best setting to differentiate physical complaints directly related to polio from midlife psychosocial stresses and physical complaints associated with physical disorders unrelated to polio. The purpose of a post-polio clinic is to provide a comprehensive evaluation for each patient and to develop a treatment plan to correct as many problems as possible including pain, weakness, joint dysfunction and equipment failure. A standardized protocol will serve as a guideline for identifying various problems. A protocol can also

*These reports were presented during a panel discussion near the end of the symposium and summarize six informal roundtable discussions held earlier in the conference.

serve to structure the gathering of data regarding the frequency of problems of these patients, allowing comparison between centers. Following is a proposed protocol for a post-polio clinic.

The general outline for the gathering of data includes:

I. History
II. Physical examination
III. Laboratory investigation
IV. Radiologic evaluation
V. Follow-up

I. History
   A. Present complaint
      1. Onset and duration, including chronological events leading up to the present problem
      2. Functional status changes as a result of the present complaint
      3. Necessary accommodations in activities of daily living, mobility, etc.
      4. Emotional impact
   B. Detailed history of the initial episode of polio
      1. Age at onset
      2. Severity and progression
      3. Compromise of ventilation
      4. Acute management
      5. Duration and characteristics of recovery phase
      6. Maximal functional recovery
   C. Chronological history of functional status
      1. Activities of daily living
      2. Social
      3. Vocational
      4. Avocational and recreational
      5. Psychological
   D. Past medical history (general)
      1. Medical
         a. Childhood and infectious diseases
         b. Diabetes, hypertension, heart disease, etc.
      2. Surgical history
         a. Orthopedic surgery for spine or extremity problems
         b. Other surgical procedures
         c. Functional gains or losses as a result of each operation

E. Family history
   1. General history of the family, including cardiovascular disease, stroke, etc.
   2. Sociological history of the family, including recent changes brought on by the patient's chief complaint

F. Review of systems
   1. Fatigue
   2. Muscle pain
   3. Fasciculations
   4. Muscle weakness or atrophy
   5. Joint pain
   6. Bulbar signs
   7. Sleep disturbance
   8. Respiratory dysfunction
   9. Exercise intolerance
   10. Autonomic dysfunction
   11. Nutritional changes
   12. Other medical symptoms

II. Physical Examination

A. General examination with special attention to
   1. Pulmonary system
   2. Cardiovascular system
   3. Peripheral vascular system
   4. Gastrointestinal system
   5. Nutritional status (skinfold measurement, weight, limb circumference, etc.)
   6. Genitourinary system (including neurological rectal examination)
   7. Skin and hair

B. Special evaluations
   1. Biomechanical evaluation
      a. Range of motion
      b. Alignment
      c. Joint stability
      d. Functional performance (station, gait, upper extremity function, etc.)
      e. Equipment assessment
   2. Neurological evaluation
      a. Manual muscle test

b. Deep tendon reflexes
c. Pathologic reflexes
d. Sensory function
e. Cranial nerve examination

3. Extended evaluation
a. Dynamometer testing
b. Cybex testing
c. Ability-agility testing
d. Timed ambulation for measured distance
e. Timed transfer activities
f. Timed activities of daily living
g. Volumetric body measurement

III. Laboratory Evaluation
A. Routine
1. CBC
2. Blood sugar
3. Lipid profile
4. Serum proteins
5. Thyroid function
6. Urinalysis
7. Pulmonary function

B. Selected tests
1. EMG with single fiber and macro testing as indicated
2. MMPI/psychometrics
3. Ultrasound
4. CT scan
5. Blood gases
6. Ear oximetry

C. Specialized tests
1. Exercise tolerance testing
2. Work capacity
3. Sleep laboratory

IV. Radiologic Evaluation
A. Routine
1. Chest
2. Cervical, thoracic and lumbosacral spine
3. Scoliosis films
4. Joints in which patient has complaints

B. Special tests
1. CT scan of spine or other body parts
2. Osteoporosis evaluation

V. Follow-up
   A. Treatment as indicated by the findings of the evaluations
   B. Monitoring of strength and functional status on a periodic basis to document improvement and/or deterioration over time.

The comprehensive evaluation of post-polio patients in a clinical setting should be an interdisciplinary effort with multiple medical and therapeutic specialists involved. In addition to the rehabilitation physician, an orthopedic consultant and pulmonary consultant should be available. Physical and occupational therapists should be involved in the physical and functional assessment of the patient and in the assessment of the equipment the patient has been using. A family service counselor should address psychological concerns and resource problems.

The findings of the interdisciplinary team should be used to diagnose the specific problems of each patient. Many conditions will be identified that can be treated relatively easily such as nerve entrapment or functional losses secondary to obesity. Other problems of weakness or functional loss may respond to a carefully designed therapy program. For those conditions that cannot be corrected, environmental adaptations or new equipment may be appropriate. All patients will benefit from the psychological support and encouragement that can be found in such a setting.

Using a questionnaire format for gathering the basic historical data described in this protocol may be helpful. If possible, the historical questionnaires developed by Halstead and others should be coalesced and expanded in a standardized fashion so that multiple centers could use the questionnaire and the results could be compared between centers. A standardized data base should be developed among cooperative centers like the one developed for the regional spinal cord injury programs.

Whenever possible, medical records should be obtained from the initial episode of polio. When this is not possible, interviewing family members may be helpful.

Standardized tests of strength, muscle bulk and function should be used whenever possible to minimize observer bias.

Outpatient evaluation of the breadth and depth described in this protocol will be quite costly. The specific testing measures to be used should be chosen in such a way as to minimize cost to the patient while gathering an adequate data base for follow-up purposes in the future.

An ethical marketing program will be necessary to attract post-polio patients to such a clinic for follow-up purposes. Many of these patients feel that they have been abandoned by the medical community because their conditions arose from illness that occurred several decades ago. The consolidation of comprehensive medical management of the late effects of polio should be attractive to post-polio people in the community once they learn of the existence of such a clinic.

Future Basic Research

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Before we address the future research plans, we must define what we should do research on. What kind of disease are we talking about? I thought I should try to answer the question of taxonomy raised earlier. From our experience of about 30 patients that we carefully examined, and from our preliminary survey of about 2,500 veterans, we have concluded that there are two subsets of problems in patients with old polio. One set includes those of musculoskeletal and general medical in nature, ie, joint pain, fatigue, decreased endurance, frequent falls and instability. These patients stabilize at a slightly diminished level of functioning and do not appear to have new lower motor neuron disease. We should not try to blame other medical problems or other neurological problems on the old polio. We should also remember that patients with old polio are not immune and perhaps have the same chances as nonpolio patients to develop other medical and neurological problems. In addition, they have problems related to chronic disability, dependency on corrective devices

and the prolonged effects of corrective surgery on the joints and spine.

The second subset of problems includes those due to new motor neuron disease that some of these patients develop. We have defined this as late progressive post-poliomyelitis muscular atrophy (PPMA). It is not amyotrophic lateral sclerosis (ALS) because patients do not have the typical ALS findings. It is not spinal muscular atrophy because spinal muscular atrophy is symmetrical and is usually bilateral, whereas PPMA is a focal disease, asymmetrical and probably progresses much more slowly than the muscular atrophies. PPMA causes new muscle weakness and wasting, and even though it is a benign form of motor neuron disease, it is a frightening experience for a post-polio victim who has already lost considerable muscle strength to the original polio.

What research should be done on PPMA? First, we should try to collect the spinal cords from patients with old polio. Dr. Tomlinson is interested in counting the neurons in various segments of the spinal cord. He can work with either frozen or paraffin blocks, although he prefers frozen. In addition, nucleic acid hybridization tests searching for polio virus should be done in the spinal cords of PPMA patients (and controls) who die from other causes. This can be done at the NIH and in several other centers in the United States.

Another future goal for PPMA is to extend our immunological and virological studies to see whether this syndrome is related to an immunological disturbance or the reactivation of the old polio virus. Our findings of a possible immunopathologic mechanism in some PPMA patients should be extended to a larger number of patients to obtain conclusive results. Future studies should include stimulation of lymphocytes from post-polio patients with polio virus to see whether they are newly sensitized to the virus and HLA typing in patients with or without symptoms to determine whether there is a genetic predisposition to development of PPMA. (The genetic background of patients without PPMA symptoms may be different from that of patients who do develop PPMA.)

We also intend to search for antibodies in the serum and spinal fluid for several common viruses and other enteroviruses including the polio virus and screen for abnormal immunoglobulins. If, indeed, our finding of abnormal immunoglobulins in cerebro-

spinal fluid is confirmed, these can be further explored by eluting the bands to see whether they represent specific antibodies to polio virus or to neuronal components.

An additional research project that should be done is to establish a model of chronic polio in monkeys. We have been thinking of doing that at the National Institutes of Health (NIH) over the last two years. It is not an easy project because the post-polio animals need a lot of care and good housing facilities in order to be maintained and followed up clinically over many years.

Another research idea is to establish an animal model for incomplete anterior horn cell disease. This could be useful in studying the (a) ability of semi-damaged anterior horn cells to sprout, (b) lifespan of a scarred anterior horn cell vs a normal one, (c) development of new weakness in limbs supplied by fewer neurons, (d) effect of aging on the ability of these cells to reinnervate surrounding muscle fibers and maintain the metabolic demands of their distal axons and (e) effect of exercise on the viability of semi-scarred or "overworking" neurons. The last will give us some clues as to how much post-polio patients should exercise and whether exercise is beneficial or detrimental, a question commonly asked by our patients who get so many different answers.

Clinical Research

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Our group discussed the clinical research questions we thought would be the most important. The first one was, what is the natural history of muscle strength in post-polio patients? There is an obvious need for a protocol that uses objective measurements that are better than manual muscle testing for longitudinal follow-up studies. Some possibilities include Cybex testing, dynamometry and evoked muscle response to electrical stimulation.

The second major research area was, what is the effect of exercise on muscles weakened by previous polio? Related to that question, what are the parameters of safe and effective exercise programs? Some of the ideas that the group generated included monitoring creatinine phosphokinase (CPK) and electromyography (EMG) changes. One participant discussed the use of 3-methylhistidine to creatinine ratios as a potential metabolic indicator of muscle damage.

The third question was, how do we classify groups of post-polio patients to study? The group seemed to agree that there are at least two major clusters of post-polio patients. One cluster consists of a large group of patients with pain and motion problems, while the other cluster consists of patients with primarily muscle weakness and fatigue. Labeling all of these problems as weakness is inadequate because weakness may also include fatigue and endurance factors. Regarding the issue of PPMA, my own impression is that atrophy is not all that prominent and the use of that term implies that anterior horn cell damage is responsible for the clinical problem. I was very impressed with Wiechers' data suggesting that there may be a peripheral defect of the axons, the terminal sprouts and the muscle fibers. So for these reasons, I am a little uneasy with the use of the term PPMA. Syndrome is an old-fashioned word describing a cluster of symptoms. This term has some potential usefulness when the symptoms included under a particular syndrome are clearly identified; therefore, I'm not sure that the use of the term syndrome should be discarded altogether.

Other important clinical research questions we discussed were:

1. What is the best way to predict the onset of later respiratory failure in old polio patients with respiratory muscle involvement?
2. How can we measure objectively muscle fatigue?
3. What is the origin of muscle pain and how can we measure it?
4. What are the habitual patterns of overuse that polio patients are doing that may be increasing their problems?
5. Are there circulatory and autonomic changes in these patients and, if so, what are their significance, especially to decreasing strength and endurance?
6. What are the effects of chronic strain on muscle and connective tissue over the years?

The second major research area was, what is the effect of exercise on muscles weakened by previous polio? Related to that question, what are the parameters of safe and effective exercise programs? Some of the ideas that the group generated included monitoring creatinine phosphokinase (CPK) and electromyography (EMG) changes. One participant discussed the use of 3-methylhistidine to creatinine ratios as a potential metabolic indicator of muscle damage.

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6. What are the effects of chronic strain on muscle and connective tissue over the years?

also needed. Dr. Stolov suggested contacting the program chairmen of the various national organizations about including a half-day symposium on the late effects of poliomyelitis during the national conferences. Also suggested was that news briefs be sent to journals such as the *Journal of the American Medical Association, Archives of Physical Medicine and Rehabilitation, Archives of Neurology* and state medical journals to reach those physicians who belong to the state medical associations, but not to the American Medical Association. Nancy Frick emphasized the need to organize post-polio support groups at the grass roots level.

Plans for Collaborative Studies

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The Mayo Clinic participants and the Manitoba participants plan to do a study of the epidemic years, at the same time comparing rural and urban populations who had polio. Dr. Aniansson from Sweden and Dr. Halstead from Houston discussed reviewing 75 polio patients between the ages of 40 and 65. Collaborative studies are needed to standardize polio protocols throughout the world, including standard measurements and clinical evaluations. Dr. Larsen from Denmark is interested in collaborating with someone on the functional and social aspects of polio. The Swedish participants would like to compare EMG patterns with another group doing electromyographical studies of post-polio patients and compare the "pain syndrome" seen in Sweden to the pain complaints of post-polio patients seen in the United States. Other suggestions were a review of muscle transfer techniques in polio patients and a study of standardized training on Cybex exercise equipment. I am interested in seeing someone investigate the acute epidemic of more than 100 polio cases occurring near the Mexico-United States border this year. We could benefit from studying this new group of polio patients using current diagnostic and follow-up procedures.

Plans for Future Meetings

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Primarily two options were discussed concerning future meetings to follow up the symposium held this weekend. We need to accommodate the many patients who inquired about attending the present meeting. One option is a presentation of the late effects of polio at the meeting sponsored by *The Rehabilitation Gazette* in St. Louis, May 10 through May 12, 1985. This presentation would make information about post-polio problems available to a broader audience, particularly former polio patients.

The other option is another meeting similar to the present one, held again here at the Roosevelt Warm Springs Institute, perhaps in the summer or fall of 1985. Physicians attending this follow-up meeting should include a broader range of specialists and generalists—surgeons, family physicians and others who are puzzled by the questions they are getting from their post-polio patients.

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