

Late Effects of Polio

Polio was considered to be a chronic, yet stable disease once the acute phase was over and rehabilitation had restored a greater or lesser degree of function. Medical textbooks have until recently described polio as having three distinct stages: acute illness, period of recovery and stable disability. However, it is now known many polio survivors develop new symptoms after decades of stable functioning. In reviewing this topic, it is necessary to provide a brief historical background to the “Late Effects of Polio” (LEOP). The most appropriate diagnostic labels to use and the proposed aetiologies of the fourth stage of polio will then be considered.

Historical Background

It has been recognised for more than 100 years that new muscle weakness can occur in survivors of polio many years after their initial illness. The first descriptions were published in the French medical literature in 1875 by Jean-Martin Charcot. Since this time, other sporadic reports have appeared in the literature describing new weakness, atrophy and fasciculations occurring years after an episode of acute paralytic poliomyelitis.³⁸ It was not until the early 1980s however, that LEOP became widely acknowledged.

By 1984, a growing awareness of LEOP prompted researchers to organise an international conference at the Warm Springs Institute for Rehabilitation in the United States of America. The term “Post-Polio Syndrome” was coined around this time. The second international meeting was held at the Warm Springs Institute in 1986 and in the following years there was a dramatic increase in clinical research into the long-term effects of polio.²⁵

In 1994, the New York Academy of Sciences and the National Institute of Health co-sponsored another international meeting that culminated in the publication of a special issue of the Annals of the New York Academy of Sciences: “The Post-Polio Syndrome: Advances in Pathogenesis and Treatment”. This conference signalled the acceptance of post-polio syndrome as a legitimate clinical entity.³⁹

Nomenclature and Definitions

There is disagreement in the literature regarding the most appropriate diagnostic labels to describe the new health problems being experienced by people with a past history of polio. The reasons for this lack of consensus are that:

- The various descriptive terms have lacked specific diagnostic criteria;
- There is currently no pathognomonic test for the condition; and
- Understanding of the underlying pathophysiology of the condition is incomplete.

The terms that have been most frequently used in the literature include “The Late Effects of Polio”, “Post-Polio Syndrome” and “Post-Polio Muscular Atrophy”.

The Late Effects of Polio (LEOP)

LEOP refers to the myriad of symptoms that individuals with a history of polio may experience. The features of LEOP can be considered in three broad categories. These include:-

1. Symptoms that can be attributed directly to damage caused by the poliovirus, including:
 - Residual weakness;
 - Musculoskeletal imbalance;
 - Growth retardation;
 - Skeletal deformities of affected limbs;
 - Respiratory insufficiency; and
 - Cold intolerance due to circulatory disturbances.

2. Symptoms thought to be related to the body’s failure to maintain the level of recovery that was achieved following the infection, such as new weakness and fatigue – The Post-Polio Syndrome.
3. Symptoms that result from secondary trauma, including:
 - Compression neuropathy, e.g. carpal tunnel syndrome after years of crutch walking;
 - Degenerative arthritis of joints that have been over-stressed due to compensatory body mechanics; and
 - Other repetitive motion problems such as tendonitis, bursitis and failing joint fusions.

Post-Polio Syndrome (PPS)

There have been many definitions of Post-Polio Syndrome (PPS) and there is still no widely agreed definition. Lauro Halstead, one of the leading researchers in this field, first proposed a definition for PPS approximately 15 years ago. He has continued to refine his definition of PPS over the years and in a more recent publication proposed the following definition:³⁹

“Post-Polio Syndrome is a neurologic disorder that produces a cluster of symptoms in individuals who had paralytic poliomyelitis many years earlier. Because these symptoms tend to occur together, they are called a syndrome. Typically, these problems occur after a period of functional and neurological stability of at least 15 years following the initial episode of poliomyelitis and include new weakness, fatigue, decreased endurance and loss of function. Some researchers also add pain as part of the syndrome, especially in muscles and joints. Less commonly, the symptoms include muscle atrophy, breathing and swallowing difficulties and cold intolerance.”

Mulder, Rosenbaum and Layton initially proposed specific criteria for the diagnosis of PPS in 1972.⁴⁰ These criteria were further refined by Halstead⁴¹ in 1991 and are outlined in Table 2.

1. A prior episode of paralytic polio confirmed by history, physical examination and typical findings on EMG.
2. Standard EMG evaluation demonstrated changes consistent with prior anterior horn cell disease.
3. Characteristic pattern of recovery – a period of neurological recovery followed by an extended interval of neurological and functional stability preceding the onset of new weakness, the interval of neurological and functional stability usually lasts 15 years or more.
4. The gradual or abrupt onset of new weakness in polio-affected muscles. This weakness may or may not be accompanied by new problems such as generalised fatigue, muscle atrophy, joint and muscle pain, decreased endurance and diminished function.
5. Exclusion of medical, orthopaedic and neurological conditions that may be causing the health problems listed in number 4 above.

The term “Post-Polio Syndrome” has developed sufficient specificity to be clinically useful and as a result, is gaining international acceptance. It has been suggested that the diagnosis of PPS should not be used indiscriminately for every person with a history of paralytic polio with a new complaint.⁵ Instead, the diagnosis of PPS should be reserved for those individuals whose symptomatology indicates motor unit dysfunction with variable musculoskeletal overuse. This opinion is further supported by Dr Pesi Katrak, Consultant in Rehabilitation Medicine, Senior Staff Specialist at Prince Henry and Prince of Wales Hospitals, Sydney. (See panel below for Dr Katrak’s comments)

Dr Pesi Katrak's comments in regard to the definition and diagnosis of PPS:

Whilst this definition of PPS is comprehensive, it includes symptoms such as muscle pain, joint pain and decreased function, which can occur as a result of mechanical factors in polio clients who have residual muscle weakness. Such musculo-skeletal problems would be expected to occur in these clients with advancing years, as indeed they would in non-polio subjects who may have a similar degree of weakness or skeletal abnormalities from any other condition. If the definitions of Mulder or Halstead are applied strictly, symptoms such as pain or declining function, which can be explained on a mechanical basis, should be considered as an "other orthopaedic condition" and hence should not be attributed to PPS.

The majority of clients present with complaints of declining function, tiredness, pain and a variety of other symptoms. In most instances, a detailed history and clinical examination, points to factors other than the PPS, which would account for the presenting symptoms. For instance:

- *Clients who have an asymmetry in limb lengths will almost inevitably suffer from degenerative or osteoarthritic changes in various major joints in the limbs and in the spine because of abnormal stresses on these structures with the passage of time. This together with the increased incidence of osteo-arthritis that occurs with increasing age results in pain and declining functional ability.*
- *It is generally accepted that physiologically there is a gradual decline in muscle strength with increasing age. Polio clients who have a moderate or severe degree of residual muscle weakness after recovery from the initial illness may find that the small amount of increase in weakness, related to age can result in a greater than anticipated decline in their ability to perform a variety of tasks. Clients will frequently perceive such a decline in function, as new weakness.*
- *Because of increased pain with physical activity or fear of falling from muscle weakness, clients tend to assume a more sedentary lifestyle and this can compound the problem of weakness due to relative disuse.*
- *Weight gain resulting in obesity and abnormal gait pattern due to focal weakness or asymmetry of limbs can often contribute to tiredness because of the increased energy requirements for carrying out day to day activities in the presence of such abnormalities.*

The diagnostic term I use for these clients, is Polio Related Problems (PRP). The term Late Effects of Polio (LEOP) would be equally acceptable.

The term PPS has been used by some clinicians to encompass many new symptoms in clients who suffered polio infection many years ago. Dr Lauro Halstead from the National Rehabilitation Hospital in Washington D.C., who has worked in this field for many years, recently noted that PPS is over diagnosed. I believe PPS is over diagnosed because of a variable interpretation of the diagnostic criteria.

My clinical impression from assessment of several hundred polio clients presenting with new symptoms is that only a very small proportion, around 15%, have PPS, i.e. progressive new weakness or excessive fatigue, which can not be explained on any other basis. I apply the diagnosis of PPS to only those clients who have a clear history of progressive new weakness or tiredness, where these symptoms cannot be explained by other factors.

Thus, whenever I see a symptomatic polio client, I try to decide whether the client's complaints are due to Post-Polio Syndrome or whether they are from Polio Related Problems. Sometimes this distinction is extremely difficult to make.

Progressive Post-Polio Muscular Atrophy (PPMA)

Progressive Post-Polio Muscular Atrophy is defined as:

“Progressive new weakness and atrophy in muscles with clinical or subclinical signs of chronic partial denervation/reinnervation compatible with previous acute polio.”

This term was coined by Dalakas and colleagues (1986)²⁸ to distinguish new, slowly progressive muscle weakness that is neurological in origin, from musculoskeletal problems or degeneration problems or both. PPMA is considered to refer to only a subgroup of those suffering from PPS.⁵ The term PPMA is less often used today, giving way to the term PPS.

In summary, there is currently no consistently agreed upon diagnostic name for the new health problems associated with former polio. There are currently no pathognomonic tests available and firm diagnostic criteria have not been established.

In the review of post-polio which follows, the term Late Effects of Polio (LEOP) will be used when discussing the myriad of problems that individuals with a history of polio often experience. Post-polio syndrome (PPS) will be used to describe the new neurological problems of fatigue and weakness that polio survivors are experiencing many years after their original illness.

Epidemiology of Post-Polio Syndrome

Epidemiological studies have reported varying estimates of the incidence of PPS depending on the criteria that were used to define the condition. A study by Codd and his colleagues (1985)⁴² found that 22.4 percent of patients with previous paralytic polio developed new symptoms. A further study by Windebank and colleagues (1991)⁴³ of the same group, found that 64 percent had developed new symptoms and 44 percent had reported new weakness. Further studies have yielded results ranging from 28 percent⁴⁴ to 42 percent.⁴⁵

The time period between acute polio and the onset of PPS has ranged from 8 to 71 years.⁴⁶ In various studies, the average interval has been found to be around 35 years.^{46,47}

Risk Factors

A number of surveys of new health problems in late polio have included an analysis of potential risk factors, but no firm conclusions were drawn. There are several reasons for this. Firstly, there have only been a small number of studies examining this area and their results have been conflicting. Secondly, due to methodological differences, e.g. the definition of PPS used to identify subjects, it is difficult to compare the findings of these studies. The risk factors that have been considered in surveys of polio survivors include:

Risk factors related to the acute polio episode:

- Age at onset^{43,48-50}
- Severity of paralysis^{43,44,48-52}
- Use of ventilator^{49,52}
- Hospitalisation^{49,52}
- Year of acute polio infection⁴⁹
- Gender^{44,48-50,52}

Risk factors related to the post-polio period:

- Polio to post-polio interval^{43,44,48}
- Current age^{43,48,49}
- Functional recovery and residual impairment^{45,48}
- Weight gain⁴⁸
- Presence of muscle pain associated with exercise⁴⁸

On the basis of these studies the most important risk factor appears to severity of the acute polio illness.

Progression

LEOP has only been widely recognised for a short period of time. As a result, studies that have investigated the progression of symptoms are limited in number and have tended to focus mainly on the progression of muscle weakness.

Dalakas and colleagues (1986)²⁸ followed a group of post-polio subjects over an average period of 8.2 years and examined the progression of new weakness. Using manual muscle testing (MRC scale) they found that the pace of worsening differed from subject to subject, being generally slow and variable even within the same subject. Long periods (up to 10 years) of stability were not uncommon. However, for a cumulative 10-year period, the average progression of weakness was estimated as one percent per year. They reported that the subjects' gender, age at onset of new symptoms and physical activity level preceding the development of new weakness did not appear to contribute significantly to the rate of progression. They also commented that the impact of the new weakness on the functional capabilities of the individual is variable, but appears to depend mostly on the residual deficit the person is left with. The more severe the residual polio deficit following the acute illness, the greater the functional impact of new weakness on the individual's neuromuscular function.

A more recently published study by Grimby and colleagues (1998)⁵³ investigated quadriceps muscle strength in 30 legs in 21 post-polio subjects over a period of eight years. All limbs tested had EMG evidence of previous polio. On average, there was a decrease in isometric muscle strength of nine percent, in isokinetic strength at 60°/s angle velocity of 13 percent and in isokinetic strength at 180°/s angle velocity of 15 percent. They divided the legs into those in which increased muscle weakness had been perceived during the eight-year period (unstable) (n= 20) and those with no perceived new weakness (stable) (n=10). The decrease during the eight years was 12-19 percent for the three strength measures in the unstable legs and 1-7 percent in the stable legs. This was contrasted with a reduction of 4-8 percent over an eight-year period in healthy controls.

A group of 50 subjects from the Mayo Clinic, who had previously been studied by Windebank and colleagues (1991)⁴³ were re-examined five years later by Windebank, Litchy, Daube and Iverson (1996).⁵⁴ This group of 50 paralytic polio survivors were investigated on both occasions using a structured history questionnaire, scored neurological examination, detailed electrophysiological studies, isometric muscle strength measurement, pulmonary function tests, psychological inventories and timed tests of function including gait and upper limb dexterity. All measures of neuromuscular function demonstrated stability over the five-year period in this group of subjects.

Stanghelle and Festvag (1997)⁵⁵ investigated progression of symptoms over a three to five year period in a group of 63 subjects who had all received a diagnosis of PPS based on the criteria proposed by Halstead and Rossi (1987).⁵² All subjects had previously received comprehensive multidisciplinary assessment and intervention. The subjects answered a questionnaire about their subjective symptoms, medical and social situation, and underwent spirometry and symptom-limited exercise stress testing. Seventy-five percent of subjects reported new weakness in polio-affected muscles during the follow-up period. General fatigue was an increasing problem in 77 percent of subjects and 61 percent reported increased muscle and joint pain during the follow-up period. A pronounced reduction in peak oxygen uptake (compared to normal values) was seen at the first evaluation. At the second examination, peak oxygen uptake was decreased further than predicted by increasing age.

While studies of muscle weakness in post-polio groups have shown relatively slow rates of progression, the study by Stanghelle and Festvag (1997)⁵⁵ points to a more alarming deterioration in subjective symptoms, physical disability, and cardiorespiratory fitness in post-polio individuals despite comprehensive multidisciplinary intervention. These findings were in contrast with those of Windebank and colleagues (1996)⁵⁴ who reported stability on a range of measures over a five-year period. Stanghelle and Festvag (1997)⁵⁵ acknowledged that their sample consisted of subjects who had already been diagnosed with PPS and thus the extent of progression in these subjects could not be extrapolated to the polio population in general. Obviously further research is required to establish the likely prognosis for individuals with a history of polio.

Aetiology of Post-Polio Syndrome

The pathological changes that produce the symptoms of post-polio syndrome are not well understood, but several theories have been developed over the years (Table 3).

Table 3: Proposed Aetiologies of PPS⁵

1. Motor unit dysfunction – degenerative changes within motor units
2. Muscle overuse
3. Muscle disuse
4. Loss of motor units with ageing
5. Predisposition to motor neuron degeneration because of glial, vascular, and lymphatic changes caused by acute polio
6. Chronic poliovirus infection or virus reactivation
7. An immune mediated syndrome
8. The effect of growth hormone
9. The combined effects of disuse, overuse, pain, weight gain or other illnesses

These theories will be briefly explained.

Motor Unit Dysfunction – Degenerative Changes Within Motor Units

Theory:

The new weakness and fatigue characteristic of PPS are due to degenerative changes in motor units, particularly loss of terminal axonal sprouts (peripheral disintegration).

Research:

This phenomenon, which occurs during recovery from paralytic polio (i.e. sprouting from surviving motor neurons leading to reinnervation of muscle fibres), is well documented. There is now considerable evidence that suggests that the abnormally enlarged motor units that develop after acute paralytic polio are not indefinitely stable.

Conventional electromyographic observations on post-polio muscles show that muscles which become extremely weak and atrophic have few to no motor unit action potentials (MUAPs), while other muscles, including those that are clinically normal or historically not affected, have large, polyphasic MUAPs.^{17,27} This is expected when one considers the generalised nature of the acute illness. The size of the voluntary motor unit action potentials are increased due to a very successful reinnervating process that results in giant-size motor units.⁵⁶

In a study comparing the size of MUAPs in control subjects and post-polio subjects with and without new weakness, Agre and Rodriquez (1990)¹⁷ found that the size of MUAPs was significantly larger in all post-polio subjects, and that those with new weakness had larger units than those without.

Wiechers and Hubbell (1981)¹⁶ first proposed that the abnormally enlarged motor units that develop after acute paralytic polio are not indefinitely stable, but that terminal axonal sprouts degenerate over time producing denervation of muscle fibres. It is possible that some of these denervated muscle fibres may become reinnervated by sprouts from neighbouring motor neurons, producing a continuous “remodelling” process of the post-polio motor units.

Many researchers now agree that this ongoing denervating and re-reinnervating process stresses the motor neurons, which after a number of years appear to lose their ability to maintain the metabolic demands of all their sprouts. Consequently, there is slow deterioration of some nerve terminals. As axonal sprouts die, some muscle fibres become permanently denervated and the post-polio individual experiences new weakness and other symptoms of neurological dysfunction.^{5,7,56} This process is illustrated in Figure 1 (page 4). Several electrophysiological and muscle biopsy studies have provided further evidence of neuromuscular transmission abnormalities and muscle fibre denervation in post-polio subjects.^{18,28,57}

New weakness in PPS can be explained on the basis of the reduced size of the motor unit when the reinnervation cannot keep pace with the ongoing denervation.⁵⁶ Trojan and Cashman (1997)⁹ hypothesised that if terminal axonal degeneration is the cause of new weakness in PPS, it is likely that there is a period of terminal axonal dysfunction that may precede degeneration by months to years. They believe that muscle fatigue in PPS can be attributed to neuromuscular junction transmission defects.

Muscle Overuse

Theory:

Enlarged motor units supplying post-polio muscles cannot indefinitely maintain the increased metabolic activity needed. As a result, overused motor units eventually degenerate, resulting in slowly increasing weakness and rapid fatiguing of muscles.

Research:

Increased creatinine kinase (CK) levels have been found in symptomatic subjects after polio, but not in equally weak asymptomatic subjects after polio.⁵⁴ Waring and McLaurin (1992)⁵⁸ found CK levels to be significantly correlated with distance of ambulation in post-polio subjects, suggesting that exercise is the cause of elevated CK in this population. Since elevated CK levels can be a marker for muscle injury, the increased CK levels may indicate muscle injury or overuse in post-polio individuals.

Perry, Fontaine and Mulroy (1995)⁵⁹ performed dynamic EMG studies during gait in post-polio subjects and found evidence of overuse in the biceps, gluteus maximus and quadriceps muscles.

Trojan and colleagues found in 1994 that muscle pain (especially that associated with exercise), joint pain, and a recent weight gain, were associated with PPS.⁴⁸ All of these factors can be markers of overuse, providing further evidence for the theory that overuse is a contributing factor to PPS. Numerous clinical studies have shown a correlation between the presence of PPS and a history of severe initial paralysis with a relatively good recovery of useful strength and function.^{48,52,60}

These observations support the theory that weakness and fatigue in PPS results from long-term substitutions for muscular weakness that place increased demands on muscles.

Muscle Disuse

Theory:

Disuse produces both deconditioning and muscle weakness in individuals.⁶¹

Research:

Post-polio subjects have been noted to have short-term increased weakness after a period of decreased activity that is secondary to illness or injury.¹⁵ The role of muscle disuse in the development of long-term weakness, however, is less clear.⁵

Loss of Motor Units with Ageing

Theory:

The natural ageing process depletes remaining anterior horn cells, leading to progressive weakness.

Research:

The normal ageing process is known to involve a gradual loss of motor neurons, but only becomes prominent after the age of 60.⁶² Several studies have failed to show a consistent correlation between the onset of new weakness and chronological age. The most consistent variable is the length of the interval between onset of polio and the appearance of new symptoms. Most subjects develop new weakness 30 to 40 years after their initial infection, and the age of onset of symptoms is variable.⁵ The superimposition of the normal ageing process on the already limited number of motor neurons present after paralytic polio may contribute to the development of PPS.⁷ The current consensus is that while chronological age may contribute to the development of new weakness, it is probably not the primary causative factor.^{5,7,56}

Less Supported Theories

Other theories that have emerged to explain the triggering mechanisms for motor unit degeneration include:

- Predisposition to motor neuron degeneration because of glial, vascular and lymphatic changes caused by acute polio – damage to the glial cells and vascular supply at the time of the acute infection can lead to secondary dysfunction of anterior horn cells.⁶³
- Chronic poliovirus infection or virus reactivation – PPS may be caused by re-exposure to live poliovirus or re-activation of persistent poliovirus in the CNS.^{28,46,64}
- An immune mediated syndrome – an ongoing inflammatory or immune response mechanism may be a precipitating factor in the development of PPS.^{5,65,66}
- The effect of growth hormone – ageing of the hypothalamus growth hormone axis may be a precipitating factor in the development of PPS.^{67,68}

While none of these theories have been completely excluded, not enough evidence exists to strongly support any of them at present.⁶⁹

The Combined Effects of Disuse, Overuse, Pain, Weight Gain or Other Illnesses

Gawne and Halstead (1995)⁵ discussed the way a number of factors may interact with each other and contribute to the development of progressive weakness and fatigue. Figure 3 is a schematic model of the possible aetiological factors for PPS and their interactions.

Chronic overuse of muscles may result in the development of new weakness, which in turn may lead to disuse. Musculoskeletal disuse leads to further weakness, atrophy, contractures, diminished endurance and weight gain. In the presence of overuse, musculoskeletal pain may occur, causing the individual to either rest, resulting in deconditioning, or compensate with improper body mechanics, leading to further overuse and possibly pain elsewhere.⁵ This complex clinical picture presents a challenge to those attempting to diagnose and manage people with the LEOP.

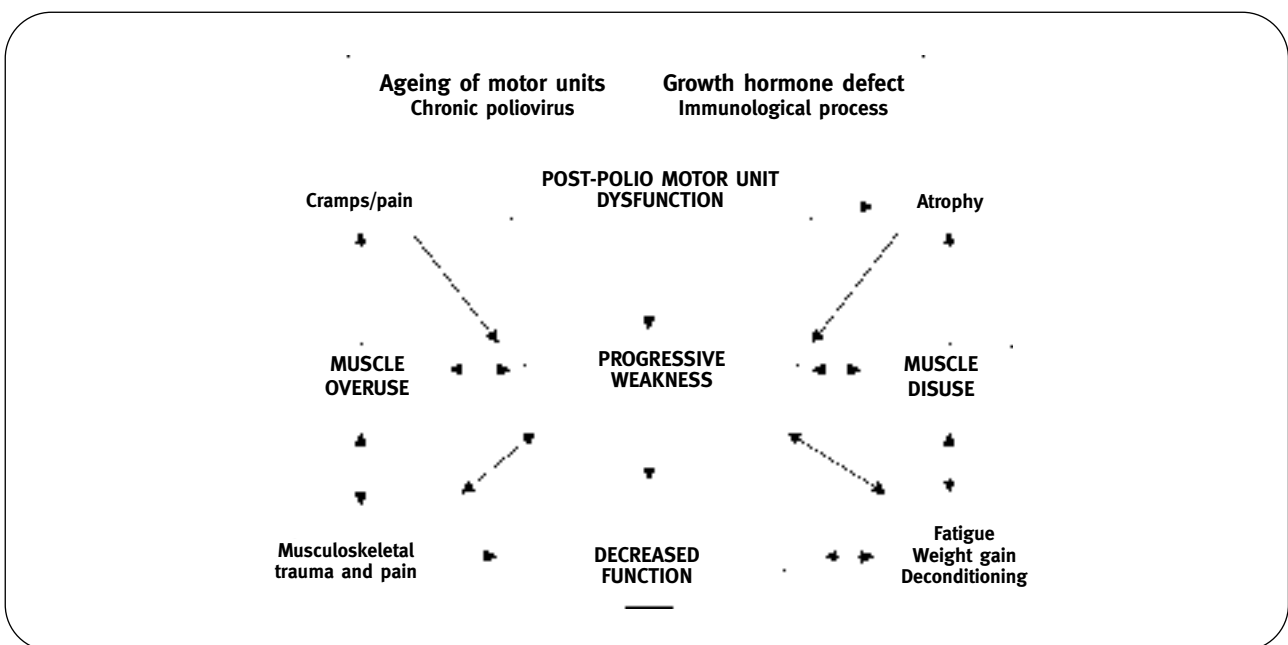


Figure 3: Schematic Model Demonstrating Possible Aetiological Factors for the Late Effects of Polio and their Interactions

(Adapted from Gawne and Halstead, 1995)⁵