



Anticholinesterases in Post-Poliomyelitis Syndrome^a

Daria A. Trojan and Neil R. Cashman

Department of Neurology
[Montreal Neurological Institute and Hospital](#)
McGill University
3801 University Street
Montreal, Quebec, H3A 2B4, Canada

Reprinted from **The Post-Polio Syndrome: Advances in the Pathogenesis and Treatment**
Volume 753 of the *Annals of the New York Academy of Sciences*
May 25, 1995

Lincolnshire Post-Polio Library copy by kind permission of Dr. Trojan

^a This work was supported in part by the Fonds de la recherche en santé du Québec, the Québec March of Dimes and the Association Polio Québec.

New weakness, fatigue, and pain after decades of functional stability in those who have recovered from acute paralytic poliomyelitis constitutes post-poliomyelitis syndrome (PPS).^[1-7] The cause of PPS is unknown, but it is thought to be due to a distal degeneration of enlarged post-polio motor units produced by terminal axonal sprouting during the recovery process after acute polio.^[8,9] The symptoms of weakness and fatigue may be a direct result of this distal motor unit degeneration;^[2,7-13] however, it is presently unclear how pain relates to disease of the motor unit. PPS is a slowly progressive motor neuron disease for which there is currently no specific treatment.^[4]

FATIGUE IN POST-POLIOMYELITIS SYNDROME

The symptom of fatigue in PPS is common, occurring in 59 to 89% of patients with new symptoms,^[1-3, 14] and is attributable to a wide variety of etiologies. It may be the most disabling symptom for patients. In PPS, patient complaints seem to suggest both a central fatigue and a peripheral fatigue.^[15] Symptoms which suggest a central fatigue include complaints of difficulties in concentration and memory, or an increased sleep requirement. Some proposed central causes of fatigue include chronic pain, "type A" behavior, depression, dysfunction of the reticular activating system, sleep disorders, and respiratory dysfunction.^[16-19] Complaints of decreased muscular endurance, or muscle fatigability (defined as increased weakness on exertion improving with rest) are suggestive of a peripheral fatigue. Proposed etiologies of peripheral fatigue include metabolic exhaustion of massively sprouted motor units, neuromuscular junction transmission defects, and overuse myopathy.^[2,20-23] A recent study showed that symptoms of generalized fatigue are as common in PPS patients as in normal controls, whereas symptoms

attributable to muscle fatigability are significantly more common in those with PPS.[24] Therefore, a peripheral fatigue may be specific for PPS, and central fatigue symptoms may occur as a result of the peripheral fatigue.

Muscle fatigability observed in PPS is similar to that seen in patients with myasthenia gravis (MG) and amyotrophic lateral sclerosis (ALS), and may be due to neuromuscular junction transmission defects. Electrophysiological evidence for neuromuscular junction transmission defects (decrement on repetitive stimulation, and increased jitter on single fiber electromyography; SFEMG) is observed in patients with MG,[25,26] ALS,[27-30] and antecedent poliomyelitis.[8,9,11,31] In MG, the neuromuscular defect is postsynaptic and occurs secondary to autoimmune destruction or blocking of muscle acetylcholine receptors.[25] In ALS and PPS, the defect is believed to be presynaptic, probably secondary to ineffective conduction along immature axonal sprouts, or to limitations in quantal number or content of acetylcholine vesicles at motor nerve terminals.[8,9,12,28-34] The oral anticholinesterase pyridostigmine, which prolongs the survival of acetylcholine at the neuromuscular junction, is useful in the treatment of muscle fatigability in MG and ALS. Because of the similar clinical and electrophysiological findings in PPS and other diseases with established neuromuscular junction pathology, anticholinesterases may be useful in the treatment of post-poliomyelitis fatigue and muscle fatigability.

RESPONSE OF SINGLE FIBER ELECTROMYOGRAPHY ABNORMALITIES IN PPS TO EDROPHONIUM

We studied the effect of the intravenous, short-acting anticholinesterase edrophonium on neuromuscular junction transmission in 17 patients with PPS.[12] No patient had concurrent medical or neurological disorders which could have interfered with the interpretation of electrophysiological testing or could be a cause of fatigue. The technique of stimulation SFEMG (S-SFEMG) was used to evaluate the neuromuscular junction in all patients. This technique allows the evaluation of the neuromuscular junction of only one muscle fiber and obviates the need for patient voluntary effort required in conventional SFEMG.[35] Like conventional SFEMG,[36] S-SFEMG allows the computation of jitter, a measure of neuromuscular junction transmission adequacy.

We performed an edrophonium test in the 17 PPS patients while recording jitter in one muscle fiber by S-SFEMG. Muscles selected (the quadriceps in 12 and the extensor digitorum communis in 5 patients) had been previously affected by acute paralytic poliomyelitis, were present in an extremity where the patient reported new muscle fatigability, and had evidence for neuromuscular junction transmission defects by conventional SFEMG. The muscle fibers selected for the edrophonium test had elevated jitter. Axonal stimulation was performed continuously at a frequency of 10 Hz during the entire period of the test. Once a suitable fiber was located in each patient, jitter measurements were obtained every 30 s for at least 3.5 min. Edrophonium (2.0 mg i.v., followed by 8.0 mg in 2 min) was then injected, and jitter was measured at the time of injection and every 30 s thereafter for at least 3.5 min. All jitter measurements obtained up to 300 s before edrophonium injection and between 30 and 300 s after edrophonium injection were used in further analyses.

We found that neuromuscular junction transmission as measured by jitter on S-SFEMG improved in a proportion of patients who underwent the edrophonium test. An example of the amelioration in jitter with edrophonium is illustrated in [FIGURE 1](#). Mean jitter pre- and post-edrophonium was compared with the unpaired *t* test. Mean jitter significantly declined in 7 patients ($p < 0.05$), was unchanged in 8 patients, and was significantly increased in 2 patients. Edrophonium-induced increased jitter has been described in MG; however, the significance of this phenomenon is unknown.[26] The finding of decreased jitter with edrophonium was not associated with pre-edrophonium jitter values, and thus the severity of the

neuromuscular junction defect (unpaired t test, $p > 0.05$). The clinical characteristics of edrophonium responders and nonresponders were compared with Fisher's exact test and Mann-Whitney U test. We found no significant differences between edrophonium responders and nonresponders in terms of age at evaluation, sex, age at acute poliomyelitis, acute poliomyelitis severity score (as measured on a 0 to 6 scale with one point being given for involvement of each of four extremities, one point for speech/swallowing dysfunction, and one point for respiratory involvement), duration of new symptoms, presence of weakness and pain, pretreatment fatigue scores (measured on a subjective 0 to 4 Hare fatigue scale/[37]), and modified Klingman mobility scores/[38] (measured on a 0 to 6 scale where 0 represents no ambulatory difficulties, 1 is mild ambulatory difficulties without need for braces, 2 is moderate ambulatory difficulties with need for braces, 3 is severe ambulatory difficulties with need for braces and a wheelchair for longer distances, 4 is nonambulatory and wheelchair bound [manual], 5 is nonambulatory and wheelchair bound [electric], and 6 is bedridden). Thus, there were no apparent distinguishing clinical and electrophysiological features of the edrophonium responders as compared to the nonresponders in our sample of patients.

FIGURE 1 Graph

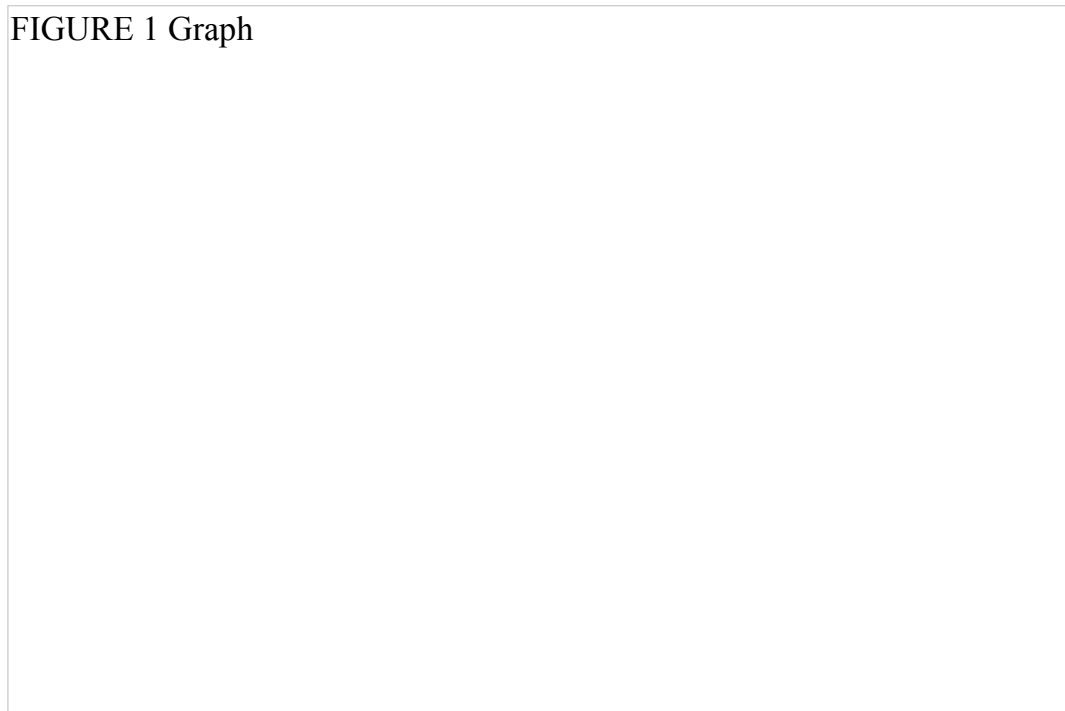


FIGURE 1. Pre- and post-edrophonium jitter as assessed by S-SFEMG in the quadriceps muscle of a pyridostigmine responder. The **upper panels** illustrate raw data; jitter is automatically computed as the mean consecutive difference between the stimulation artifact (*single arrows*) and the unstable muscle fiber potential (*double arrows*) in 50 superimposed stimulations. The **lower panels** illustrate jitter recorded every 30 s for 3.5 min before and after injection of edrophonium 10 mg i.v. This patient had a significant reduction in jitter (unpaired t test, $p < 0.05$) with edrophonium in the studied potential. (From Trojan *et al.*[12] Reprinted with permission from the *Journal of the Neurological Sciences*.)

RESPONSE OF FATIGUE IN PPS TO PYRIDOSTIGMINE

After completion of the edrophonium test, we evaluated response of fatigue to pyridostigmine.[12] Patients and treating physician were blinded to the results of the edrophonium test. All 17 patients were initiated on oral pyridostigmine at 30 mg per day, and increased every other day by 30 mg to attain a maximum dosage of 180 mg per day in three divided doses. One patient was maintained on 120 mg per

day because of side effects at a higher dose. Clinical response to pyridostigmine was assessed by evaluating fatigue and function on the subjective Hare fatigue scale,^[37] the modified Barthel ADL index,^[39] and a modified Klingman mobility index^[38] before and one month after initiation of treatment. A pyridostigmine response was defined as an improvement of at least 20% on the Hare fatigue scale over initial scores.

Side effects from the medication occurred in approximately one-half of patients, usually in the early stages of treatment, and included symptoms typical of increased cholinergic activity (diarrhea, intestinal cramps, blurred vision, increased urinary frequency, muscle cramps, and anxiety). In two patients, additional medications were started (propantheline and bethanechol) because of the development of persistent diarrhea and increased urinary frequency. One patient developed transient increased weakness, which resolved with discontinuation of the medication.

We found that subjective fatigue improved in a proportion of patients with pyridostigmine. Nine of 17 patients (53%) experienced a reduction in systemic fatigue of 20 to 88% while on the medication. All 9 patients also reported decreased muscle fatigability and the ability to perform certain activities which they had previously been unable to do. However, only 2 patients were noted to have an improvement on the functional scales used, probably because of the low responsiveness of these scales to treatment effect in this patient population. All 9 patients requested continuation of the medication (for a period of 0.3 to 2.3 years, mean 1.22 years) because of the perceived benefits derived from treatment. Pyridostigmine responders were not differentiated from nonresponders in terms of age at evaluation, sex, age at acute poliomyelitis, acute poliomyelitis severity score, duration of new symptoms, function scores, and presence of weakness and pain. However, pyridostigmine-responders were significantly more fatigued than nonresponders on the subjective Hare fatigue score before treatment (Mann-Whitney U test, $p = 0.01$).

RELATIONSHIP OF SINGLE FIBER ELECTROMYOGRAPHY STUDIES TO CLINICAL RESPONSE

We assessed the possible relationship between the edrophonium test and clinical response to pyridostigmine by three methods.^[12] First, we found that 6 of 7 patients with decreased jitter on edrophonium were less fatigued with pyridostigmine, and that 7 of 10 patients with no change or increased jitter on edrophonium did not respond to pyridostigmine (Fisher's exact test, $p < 0.04$). Thus, edrophonium response appeared to predict clinical response to pyridostigmine. Subsequently, this relationship was also separately analyzed from the perspective of pyridostigmine and edrophonium response. We found that the 7 patients who experienced significantly decreased jitter with edrophonium had a significant reduction of fatigue with pyridostigmine (mean pre-Hare fatigue score = 3.0, post- = 1.5, $p = 0.03$). The 10 patients who did not experience jitter reduction with edrophonium had a nonsignificant reduction in fatigue scores with pyridostigmine (mean pre-Hare fatigue score = 2.5, post- = 1.85, $p = 0.25$). We then compared jitter means (normalized to 100% of pre-edrophonium mean for each patient) of the 9 pyridostigmine responders to the pyridostigmine nonresponders (FIG. 2). We found a significant reduction in jitter means pre- and post-edrophonium in the 9 pyridostigmine responders (100 versus 88%, unpaired t test, Bonferroni corrected, $p < 0.001$). We also found that post-edrophonium jitter means were significantly lower in the pyridostigmine responders than those in nonresponders (101 versus 88%, $p < 0.001$). No significant difference was found between pyridostigmine nonresponder jitter means pre- and post-edrophonium. Thus, jitter response on edrophonium injection was significantly associated with clinical response to pyridostigmine.

FIGURE 2 Graph

FIGURE 2. Reduction of fatigue with pyridostigmine is associated with reduction of jitter on edrophonium injection. Pyridostigmine-responders (*open circles*) are those who report a reduction of 20% in fatigue on the Hare fatigue score with pyridostigmine 180 mg per day. Pyridostigmine-nonresponders are illustrated with *closed circles*. Jitter plots are normalized to 100% of pre-edrophonium mean jitter. A significant reduction in jitter mean is observed in pyridostigmine-responders with edrophonium (Bonferroni corrected, $p < 0.001$). The decline and subsequent increase in jitter after edrophonium injection is consistent with the known pharmacokinetics of the medication. Post-edrophonium jitter mean in pyridostigmine-responders is significantly lower ($p < 0.001$) than in nonresponders. There is no significant difference in jitter means of pyridostigmine nonresponders before and after edrophonium injection. Error bars = standard error of the mean. (From Trojan *et al.*[12] Reprinted with permission from the *Journal of the Neurological Sciences*.)

PYRIDOSTIGMINE EFFECT ON ISOKINETIC NEUROMUSCULAR FUNCTION

The effect of pyridostigmine on isokinetic neuromuscular function in 7 patients with PPS was studied by Kilfoil *et al.*[40,41] All subjects had a minimum manual muscle strength (measured on the Medical Research Council scale[42]) of 3 in the knee extensors and 2 in the knee flexors. The isokinetic dynamic fatigue protocol used consisted of 25 reciprocal, isokinetic contractions of knee extension and flexion (unilaterally), which was performed by the 7 patients and 15 normal controls. The speed of the movement and the angle of excursion were recorded simultaneously with the torque signal. Angle-specific torques (0.79 and 1.05 rads) of the quadriceps were used for subsequent analyses. This isokinetic fatigue protocol has been found to be reliable in the quadriceps in PPS patients and in normal controls.[41-43] Three baseline assessments were performed on the 7 patients while on pyridostigmine 180 mg per day. After these assessments, the fatigue protocol was again performed two more times while the subject was either on or off pyridostigmine. The sequence of the evaluations on or off pyridostigmine was randomly determined, and the evaluator was blinded to the sequence of drug withdrawal and reinitiation. Measurements off pyridostigmine were performed after discontinuation of the medication for 48 h.

The response of neuromuscular function to pyridostigmine was assessed by comparing measurements on

and off the medication. We found that total work for the 7 subjects did not differ while the patients were on or off pyridostigmine. However, on further evaluation of the data, it was apparent that the pyridostigmine response differed in groups of patients. The torque of isokinetic extension of the male patients off pyridostigmine was lower than the mean \pm 2 SD while they were on pyridostigmine. Only one of these subjects demonstrated true fatigability (defined as a greater negative slope of the regression line). The other three male subjects demonstrated less isokinetic torque while off pyridostigmine than on pyridostigmine. The three remaining female subjects did not demonstrate either true fatigability or decreased isokinetic strength while off pyridostigmine.

DISCUSSION

Evidence for neuromuscular junction transmission defects as seen by increased jitter and blocking on SFEMG is commonly observed in those who have recovered from paralytic poliomyelitis, and has been reported by many investigators.[\[7-9, 11, 12\]](#) The presence of increased jitter is not specific for PPS and is found both in patients who are stable after paralytic poliomyelitis and in those with new weakness.[\[11\]](#) Increased jitter is known to occur at all stages following recovery from paralytic poliomyelitis, and may be due to inadequate conduction along terminal axonal sprouts, or to suboptimal release of acetylcholine.[\[8, 9, 12, 33, 34\]](#) After acute paralytic poliomyelitis, recovery of muscular strength can occur by terminal axonal sprouting of surviving motor neurons, with partial or complete reinnervation of denervated muscle fibers.[\[8, 9, 44\]](#) Evidence shows that these enlarged motor units are undergoing a process of continuous remodeling, with constant denervation and reinnervation after paralytic polio.[\[8, 9, 11, 45, 46\]](#) Thus, the presence of immature terminal sprouts (which are known to have decreased conduction) at all stages following recovery from acute polio may account, at least partially, for the observed abnormal jitter. Decades after recovery, irreversible degeneration of terminal sprouts without reinnervation may account for the symptoms of fatigue and weakness observed in PPS. An early stage of this degeneration may be neuromuscular junction transmission defects.[\[12\]](#) At this time it is unclear whether neuromuscular junction transmission defects increase with the passage of time.[\[8, 9\]](#) However, there is an association between jitter and degree of initial recovery after polio as estimated by fiber density on SFEMG, macroelectromyography motor unit potential amplitudes, and fiber type grouping on muscle biopsy.[\[11, 47\]](#) Thus, the extent of recovery may determine the degree of motor unit instability later in life.

Because of the clinical and electrophysiological similarities of PPS with other known disorders of the neuromuscular junction, we assessed the effects of the intravenous, short-acting anticholinesterase, edrophonium, on jitter and of the oral, long-acting anticholinesterase, pyridostigmine, on clinical fatigue. Edrophonium has been found to improve neuromuscular junction transmission defects in MG and ALS as measured by repetitive stimulation and jitter on SFEMG.[\[26, 27, 36\]](#) An early study showed that neuromuscular junction transmission as measured by repetitive stimulation can improve with the intravenous anticholinesterase neostigmine in patients with prior poliomyelitis.[\[31\]](#) We found that neuromuscular junction transmission as measured by jitter on SFEMG improves with anticholinesterase treatment in a continuously activated muscle fiber in approximately 50% of PPS patients studied. The fact that not all neuromuscular junctions studied were ameliorated with edrophonium suggests the presence of a variety of neuromuscular junction defects in patients with past paralytic poliomyelitis. Subsequently, we treated all 17 PPS patients with pyridostigmine 180 mg per day, and found that approximately 50% of patients reported decreased general fatigue and muscle fatigability on the medication. We demonstrated a significant association between the results of the S-SFEMG/edrophonium test and clinical response to pyridostigmine. These findings indicate that neuromuscular junction transmission defects may be the cause of fatigue in at least a proportion of patients with PPS. The clinical neuromuscular response to anticholinesterases in PPS is currently unclear: preliminary studies, however, show that a proportion of patients have increased isokinetic strength on pyridostigmine as compared to off pyridostigmine, rather

than improved fatigability.[40,41] Therefore, the beneficial effects of the medication may actually be due to a greater muscular strength.

In fatigued post-poliomyelitis patients, conditions causing fatigue, such as other neurological disorders, depression, and a variety of medical conditions must be considered prior to attributing patient fatigue to PPS. If these other conditions are excluded, and consequently, if fatigue is believed to be due to PPS, then weight loss, energy conservation, better organization of daily activities, and planned short rest periods or naps during the day may be beneficial. If these measures are ineffective or insufficient, pyridostigmine therapy may be warranted. Our finding that pyridostigmine responders were more fatigued initially than nonresponders may provide some guidance in determining which patients are more likely to respond to the medication.

Anticholinesterases inhibit the hydrolysis of acetylcholine in the neuromuscular junction and prolong its effect. There are some relative contraindications to the use of pyridostigmine which include cardiac arrhythmias, bronchospasm, increased bronchial secretions, and some urological conditions. The chronic effects of anticholinesterases in PPS are currently unknown, but these medications have been used effectively in MG for decades. Anticholinesterases are associated with acute and chronic toxicities, both pre- and postsynaptic in normal experimental animals and probably in humans.[48] However, the doses that were used in animal studies and are used commonly in patients with MG are manyfold higher than the dose we have used in PPS (180 mg/day vs up to 2 g/day in MG). Pyridostigmine was recently used in soldiers involved in the Gulf War as a pretreatment to possible organophosphate intoxication. A two-week double-blinded, placebo-controlled, cross-over trial in 7 male soldiers indicated that chronic pyridostigmine administration did not negatively impact on the ability of soldiers to perform moderate physical work in a desert environment, and did not result in an increase in subjective symptoms.[49] A retrospective study of 41,650 soldiers who self-administered pyridostigmine 30 mg orally every 8 h for 1 to 7 days during Operation Desert Storm found that approximately 50% of the soldiers noted mild physiological changes (e.g., increased flatus, abdominal cramps, soft stools, and urinary urgency), 1% had side effects severe enough to warrant medical attention, and less than 0.1% discontinued the medication because of side effects. Thus, pyridostigmine could be administered to virtually all soldiers.[50] In our study, we found that acute side effects (usually increased gut motility) occurred commonly, but tended to decrease with chronic use. Even though we have not observed evidence for chronic toxicity in PPS patients in our clinic maintained for years on this low dose, it is possible that chronic use could produce permanent morphological alterations at the neuromuscular junction. We also recommend "drug holidays" in patients chronically treated with pyridostigmine, approximately every six months. Occasionally, after months or years of treatment, patients find that the medication is no longer helpful, and it is discontinued. Therefore, pyridostigmine may be helpful only in certain stages of the disease process.

CONCLUSIONS

Our studies indicate that a proportion of fatigued post-poliomyelitis patients can experience an amelioration of defects in neuromuscular junction transmission and of clinical fatigue with anticholinesterases. Because S-SFEMG response was significantly associated with clinical response to anticholinesterases, fatigue in PPS may be caused by defects in neuromuscular junction transmission in a proportion of patients. Preliminary studies in a small group of patients indicate that anticholinesterases may produce their clinical neuromuscular response by producing an increase in isokinetic strength in a proportion of patients. Our studies provide a physiological rationale for the use of anticholinesterases in PPS for the symptom of fatigue. However, further randomized, placebo-controlled, double-blinded trials are needed to establish definitively the benefits and risks of these agents.

ACKNOWLEDGMENTS

We are indebted to the patients from the [Montreal Neurological Institute and Hospital](#) post-polio clinic who donated their time to participate in our studies, and to EMG technicians Lora Tombari and Susan Murray for their expert technical assistance.

REFERENCES

1. HALSTEAD, L. S., D. O. WIECHERS & C. D. ROSSI. 1985. Late effects of poliomyelitis: A national survey. *In* Late Effects of Poliomyelitis. L. S. Halstead & D. O. Wiechers, Eds.: 11-31. Symposia Foundation. Miami, FL.
2. JUBELT, B. & N. R. CASHMAN. 1987. Neurologic manifestations of the post-polio syndrome. *Crit. Rev. Neurobiol.* **3**: 199-220. [\[PubMed Abstract\]](#)
3. CODD, M. B., D. W. MULDER, L. T. KURLAND, C. M. BEARD & W. M. O'FALLON. 1985. Poliomyelitis in Rochester, Minnesota, 1935-1955: Epidemiology and long-term sequelae. A preliminary report. *In* Late Effects of Poliomyelitis. L. S. Halstead & D. O. Wiechers, Eds.: 121-134. Symposia Foundation. Miami, FL.
4. MUNSAT, T. L., ED. 1991. Post-Polio Syndrome. Butterworth-Heinemann. Boston, MA.
5. WINDEBANK, A. J., J. R. DAUBE, W. J. LITCHY, M. CODD, E. Y. S. CHAO, L. T. KURLAND & R. IVERSON. 1987. Late sequelae of paralytic poliomyelitis in Olmsted County, Minnesota. *In* Research and Clinical Aspects of the Late Effects of Poliomyelitis. L. S. Halstead & D. O. Wiechers, Eds.: 27-38. March of Dimes Birth Defects Foundation. White Plains, NY. [\[PubMed Abstract\]](#)
6. SPEIER, J. L., R. R. OWEN, M. KNAPP & J. K. CANINE. 1987. Occurrence of postpolio sequelae in an epidemic population. *In* Research and Clinical Aspects of the Late Effects of Poliomyelitis. L. S. Halstead & D. O. Wiechers, Eds.: 39-48. March of Dimes Birth Defects Foundation. White Plains, NY. [\[PubMed Abstract\]](#)
7. DALAKAS, M. C., G. ELDER, M. HALLETT, J. RAVITS, M. BAKER, N. PAPADOPOULOS, P. ALBRECHT & J. SEVER. 1986. A long-term follow-up study of patients with postpoliomyelitis neuromuscular symptoms. *N. Engl. J. Med.* **314**: 959-963. [\[PubMed Abstract\]](#)
8. WIECHERS, D. O. & S. L. HUBELL. 1981. Late changes in the motor unit after acute poliomyelitis. *Muscle & Nerve* **4**: 524-528. [\[PubMed Abstract\]](#)
9. WIECHERS, D. O. 1988. New concepts of the reinnervated motor unit revealed by vaccine-associated poliomyelitis. *Muscle & Nerve* **11**: 356-368. [\[PubMed Abstract\]](#)
10. TROJAN, D. A., D. GENDRON & N. R. CASHMAN. 1991. Electrophysiology and electrodiagnosis of the post-polio motor unit. *Orthopedics* **14**: 1353-1361. [\[Lincolnshire Library\]](#)

[Full Text](#)

11. CASHMAN, N. R., R. MASELLI, R. L. WOLLMAN, R. ROOS, R. SIMON & J. P. ANTEL. 1987. Late denervation in patients with antecedent paralytic poliomyelitis. *N. Engl. J. Med.* **1317**: 7-12. [\[PubMed Abstract\]](#)
12. TROJAN, D. A., D. GENDRON & N. R. CASHMAN. 1993. Anti-cholinesterase responsive neuromuscular junction transmission defects in post-poliomyelitis fatigue. *J. Neurol. Sci.* **114**: 170-177. [\[Lincolnshire Library Full Text\]](#)
13. DALAKAS, M. 1991. Post-polio syndrome: Clues from muscle and spinal cord studies. In *Post-Polio Syndrome*. T. L. Munsat, Ed.: 39-65. Butterworth-Heinemann. Boston, MA.
14. TROJAN, D. A. & N. R. CASHMAN. 1989. Treatment of fatigue in the post-poliomyelitis syndrome with pyridostigmine. *Arch. Phys. Med. Rehabil.* **70**: A42 (abstr.).
15. GOW, P. J., M. STOKES, R. H. T. EDWARDS. 1987. Investigations of neuromuscular performance in post-polio patients: A practical approach. In *Research and Clinical Aspects of the Late Effects of Poliomyelitis*. L. S. Halstead & D. O. Wiechers, Eds.: 293-300. March of Dimes Birth Defects Foundation. White Plains, NY. [\[PubMed Abstract\]](#)
16. BRUNO, R. L. & N. M. FRICK. 1987. Stress and "type A" behavior as precipitants of post-polio sequelae: The Felician/Columbia Survey. In *Research and Clinical Aspects of the Late Effects of Poliomyelitis*. L. S. Halstead & D. O. Wiechers, Eds.: 145-155. March of Dimes Birth Defects Foundation. White Plains, NY. [\[Lincolnshire Library Full Text\]](#)
17. KOHL, S. J. 1987. Emotional responses to the late effects of poliomyelitis. In *Research and Clinical Aspects of the Late Effects of Poliomyelitis*. L. S. Halstead & D. O. Wiechers, Eds.: 135-143. March of Dimes Birth Defects Foundation. White Plains, NY. [\[PubMed Abstract\]](#)
18. FISCHER, D. A. 1987. Sleep-disordered breathing as a late effect of poliomyelitis. In *Research and Clinical Aspects of the Late Effects of Poliomyelitis*. L. S. Halstead & D. O. Wiechers, Eds.: 115-120. March of Dimes Birth Defects Foundation. White Plains, NY. [\[PubMed Abstract\]](#)
19. HALSTEAD, L. S. 1991. Post-polio syndrome: Definition of an elusive concept. In *Post-Polio Syndrome*. T. L. Munsat, Eds.: 23-39. Butterworth-Heinemann. Boston, MA.
20. McCOMAS, A. J., A. R. M. UPTON & R. E. P. SICA. 1973. Motor neuron disease and aging. *Lancet* **2**: 1477-1480. [\[PubMed Abstract\]](#)
21. GRIMBY, G. & G. EINARSSON. 1987. Muscle morphology with special reference to muscle strength in post-polio subjects. In *Research and Clinical Aspects of the Late Effects of Poliomyelitis*. L. S. Halstead & D. O. Wiechers, Eds.: 265-274. March of Dimes Birth Defects Foundation. White Plains, NY. [\[PubMed Abstract\]](#)
22. MUNSAT, T. L., P. ANDRES & L. THIBIDEAU. 1987. Preliminary observations on long-term muscle force changes in the post-polio syndrome. In *Research and Clinical Aspects of the Late Effects of Poliomyelitis*. L. S. Halstead & D. O. Wiechers, Eds.: 329-334. March of Dimes Birth Defects Foundation. White Plains, NY. [\[PubMed Abstract\]](#)
23. PERRY, J., G. BARNES & J. K. GRONLEY. 1988. The postpolio syndrome: An overuse phenomenon. *Clin. Orthop. Relat. Res.* **233**: 145-162. [\[Lincolnshire Library Full Text\]](#)
24. BERLLY, M. H., W. W. STAUSER & K. M. HALL. 1991. Fatigue in postpolio syndrome. *Arch. Phys. Med. Rehabil.* **72**: 115-118. [\[PubMed Abstract\]](#)
25. ENGEL, A. G. 1986. Acquired autoimmune myasthenia gravis. In *Myology*. A. G. Engel & B. Q. Banker, Eds.: 1925-1954. McGraw-Hill Inc. New York.
26. STALBERG, E., J. EKSTEDT & A. BROMAN. 1974. Neuromuscular transmission in myasthenia gravis studied with single fiber electromyography. *J. Neurol. Neurosurg. Psychiatry* **37**: 540-547. [\[PubMed Abstract\]](#)
27. MULDER, D. W., E. H. LAMBERT & L. M. EATON. 1959. Myasthenic syndrome in patients with amyotrophic lateral sclerosis. *Neurology* **9**: 627-631.

28. DENYS, E. H. & F. H. NORRIS. 1979. Amyotrophic lateral sclerosis impairment of neuromuscular transmission. *Arch. Neurol.* **36**: 202-225. [[PubMed Abstract](#)]
29. BERNSTEIN, L. P. & J. P. ANTEL. 1981. Motor neuron disease: Decremental response to repetitive nerve stimulation. *Neurology* **31**: 204-207. [[PubMed Abstract](#)]
30. STALBERG, E., M. S. SCHWARTZ & J. V. TRONTELJ. 1975. Single fiber electromyography in various processes affecting the anterior horn cell. *J. Neurol. Sci.* **24**: 403-415. [[PubMed Abstract](#)]
31. HODES, R. 1948. Electromyographic study of defects of neuromuscular transmission in human poliomyelitis. *Arch. Neurol. Psychiatry* **60**: 457-473.
32. BRADLEY, W. G. 1987. Recent views on amyotrophic lateral sclerosis with emphasis on electrophysiological studies. *Muscle & Nerve* **10**: 490-502. [[PubMed Abstract](#)]
33. TROJAN, D. A., D. GENDRON & N. R. CASHMAN. 1993. Stimulation frequency-dependent neuromuscular junction transmission defects in patients with prior paralytic poliomyelitis. *J. Neurol. Sci.* **118**: 150-157. [[Lincolnshire Library Full Text](#)]

34. MASELLI, R. A., C. A. DAVIS, R. WOLLMAN, C. G. LEUNG, E. F. SALAZAR-GRUESO & R. F. ROOS. 1992. Neurophysiological and morphological abnormalities at the neuromuscular junction in patients with post-poliomyelitis syndrome. *Neurology* **42(Suppl. 13)**: 231(abstr.).
35. TRONTELJ, J. V., M. MIHELIN, J. M. FERNANDEZ & E. STALBERG. 1986. Axonal stimulation for end-plate jitter studies. *J. Neurol. Neurosurg. Psychiatry* **49**: 677-685. [[PubMed Abstract](#)]
36. STALBERG, E. & J. V. TRONTELJ. 1979. *Single fibre electromyography*. The Mirvalle Press Limited. Old Woking, Surrey, UK.
37. HARE, T. W., A. H. HAKKI, D. T. LOWENTHAL, A. S. ISKANDRIAN & B. L. SEGAL. 1985. Simplified scale for rating perceived exertion in patients with coronary artery disease. *Ann. Sports Med.* **2**: 64-68.
38. KLINGMAN, J., H. CHUI, M. CORGIAT & J. PERRY. 1988. Functional recovery: A major risk factor for development of postpoliomyelitis muscular atrophy. *Arch. Neurol.* **45**: 645-647. [[PubMed Abstract](#)]
39. GRANGER, C. V. 1982. Health accounting: Functional assessment of the long-term patient. *In* Krussen's Handbook of Physical Medicine and Rehabilitation. F. J. Kottke, G. K. Stilwell & J. F. Lehmann, Eds.: 253-274. W. B. Saunders. Philadelphia, PA.
40. KILFOIL, M., D. M. M. ST. PIERRE, D. A. TROJAN & N. R. CASHMAN. 1992. The effects of pyridostigmine (Mestinon) on isokinetic evaluation of fatigue in subjects with post-poliomyelitis syndrome. *Physical Ther.* **72**: S112. (abstr.)
41. KILFOIL, M., D. M. M. ST. PIERRE, D. A. TROJAN & N. R. CASHMAN. 1994. Reliability of isokinetic evaluation of neuromuscular fatigue and the effects of pyridostigmine on subjects with post-poliomyelitis syndrome: A pilot study. Submitted.
42. MEDICAL RESEARCH COUNCIL. 1982. Aids to the examination of the peripheral nervous system. 1. Her Majesty's Office. London.
43. KILFOIL, M. R., D. M. M. ST. PIERRE. 1993. Reliability of Cybex II isokinetic evaluations of torque in post-poliomyelitis syndrome. *Arch. Phys. Med. Rehabil.* **74**: 730-735. [[PubMed Abstract](#)]
44. COERS, C. & A. L. WOOLF. 1959. *The innervation of muscle; a biopsy study*. Blackwell Scientific. Oxford.
45. LANGE, D. J., T. SMITH & R. E. LOVELACE. 1989. Postpolio muscular atrophy: Diagnostic utility of macroelectromyography. *Arch. Neurol.* **46**: 502-506. [[PubMed Abstract](#)]
46. RAVITS, J., M. HALLETT, M. BAKER, J. NILSSON & M. DALAKAS. 1990. Clinical and electromyographic studies of post-poliomyelitis muscular atrophy. *Muscle & Nerve* **13**: 667-674. [[PubMed Abstract](#)]
47. MASELLI, R. A., N. R. CASHMAN, R. L. WOLLMAN, E. F. SALAZAR-GRUESO & R. ROOS. 1992. Neuromuscular transmission as a function of motor unit size in patients with prior

- poliomyelitis. *Muscle & Nerve* **15**: 648-655. [[PubMed Abstract](#)]
48. MUNSAT, T. L. 1984. Anticholinesterase abuse in myasthenia gravis. *J. Neurol. Sci.* **64**: 5-10. [[PubMed Abstract](#)]
49. COOK, J. E., B. WENGER & M. A. KOLKA. 1992. Chronic pyridostigmine bromide administration: Side effects among soldiers working in a desert environment. *Military Med.* **157**: 250-254.
50. KEELER, J. R., C. G. HURST & M. A. DUNN. 1991. Pyridostigmine used as a nerve agent pretreatment under wartime conditions. *JAMA* **266**: 693-695. [[PubMed Abstract](#)]

[▲ Top of Article ▲](#)

[Content Catalogue](#) [Source Catalogue](#)

[Reception](#)

[Library](#)

[Networking](#)

[Directory](#)

[What's New?](#)

[The Lincolnshire Post-Polio Network](#)

Registered Charity No. [1064177](#)

An Information Service for Polio Survivors and Medical Professionals

All enquiries, book requests, medical article requests, membership fees, items for newsletters and donations to

**The Secretary, Lincolnshire Post-Polio Network
PO Box 954, Lincoln, Lincolnshire, LN5 5ER United Kingdom**

Telephone: [+44 \(0\)1522 888601](#)

Facsimile: [+44 \(0\)870 1600840](#)

Email: info@lincolnshirepostpolio.org.uk

Web Site: www.lincolnshirepostpolio.org.uk

The Lincolnshire Post-Polio Network takes great care in the transcription of all information that appears at this site. However, we do not accept liability for any damage resulting directly or otherwise from any errors introduced in the transcription. Neither do we accept liability for any damage resulting directly or otherwise from the information available at this site. The opinions expressed in the documents available at this site are those of the individual authors and do not necessarily constitute endorsement or approval by the Lincolnshire Post-Polio Network.

© Copyright The Lincolnshire Post-Polio Network

Copyright is retained by The Lincolnshire Post-Polio Network and/or original author(s). Permission is granted to print copies of individual articles for personal use provided they are printed in their entirety. Links from other Internet WWW sites are welcome and encouraged. We only ask that you let us know so that we can in future notify you of critical changes. Reproduction and redistribution of any articles via any media, with the exception of the aforementioned, requires permission from The Lincolnshire Post-Polio Network and where applicable, the original author(s).

Document preparation: Chris Salter, [Original Think-tank](#), Cornwall, United Kingdom.

Document Reference: <URL:<http://www.zynet.co.uk/ott/polio/lincolnshire/library/trojan/anticholinesterases.html>>

Created: 7th August 1998

Last modification: 30th January 2010.

