

Post-Polio Motor Neurons and Units: What We Know for Sure

Neil R. Cashman, MD, University of Toronto, Toronto, Canada

Motor neurons are located in the brainstem and spinal cord. They send long processes called axons out to the muscle. In the muscle, the axon divides into terminal axonal branches that contact muscle fibers to trigger their contraction. The terminal axons communicate with the muscle fibers at the neuromuscular junction through release of acetylcholine, a chemical compound synthesized by motor neurons.

A normal motor neuron innervates from a few to thousands of muscle fibers, depending on the muscle. An eye muscle, for example, needs few muscle fibers compared with a leg muscle that may need up to 5,000 muscle fibers per motor neuron. A motor unit is defined as a motor neuron and all the muscle fibers it supplies.

Part of the recovery process from acute poliomyelitis involves terminal axonal sprouting of remaining healthy motor neurons to reinnervate muscle fibers that have become denervated by destruction of their motor neurons. These axonal sprouts can dramatically increase the number of muscle fibers innervated by the same motor neuron – in some cases, as many as seven to eight times normal.

This arrangement, good as it is over the short term, is not indefinitely stable. Over time, muscle fibers begin to lose their innervation. Imagine, for example, a tree trunk with many branches that has eight or nine times as many branches grafted onto it. The tree may be able to support those extra branches for a period of

time, but eventually they may begin to degenerate or fall off. This process is what we think is going on in post-polio syndrome, first proposed by David Wiechers, MD, and Susan Hubble, MD, in 1981.

What evidence do we have that supports that hypothesis? Muscle biopsies provide the strongest indication that there is some ongoing, terminal axonal degeneration. But listening over the years to people having this problem, my colleagues and I have concluded that post-polio syndrome is not simply a disease of slowly progressive new weakness.

We have proposed that the complaints – fatigue, lack of endurance, and a whole list of other symptoms originally collated by

Mary Codd, MD, when she was doing her work with Anthony Windebank, MD, at the Mayo Clinic – that wax and wane and can change from hour to hour or day to day or week to week are due to dysfunction in terminal axons rather than degeneration. If a terminal axon is in the process of degenerating, it is not here one day and gone the next. During an intervening period, the axon is not functioning 100%, but it is still there.

What is the evidence of axonal dysfunction? Electromyography can demonstrate a muscle that has been stimulated very rapidly, but then loses its force into the stimulation. If we stopped and waited a couple of minutes, the

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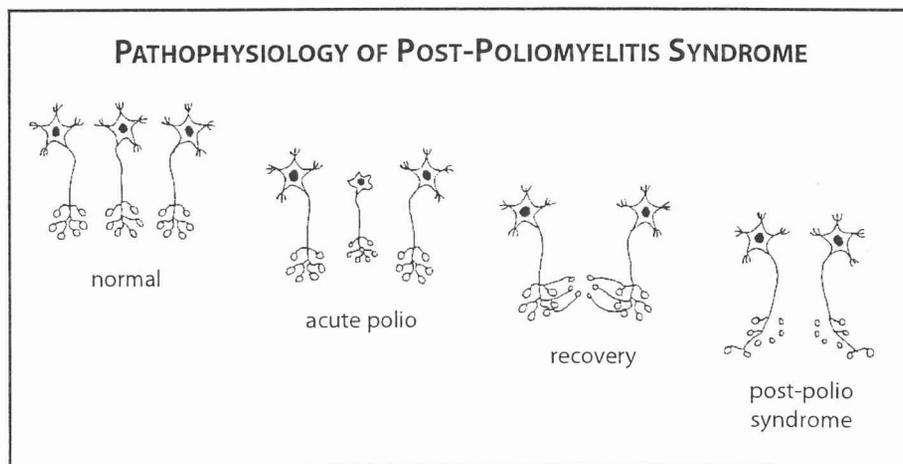


Figure 1. Normal: Three normal motor units are presented. **Acute Polio:** Invasion of one motor neuron by poliovirus produces degeneration of the affected motor neuron and denervation of associated muscle fibers. **Recovery:** Recovery after paralytic polio occurs through axonal sprouting from surviving motor neurons with reinnervation of muscle fibers. Muscle fiber hypertrophy may also occur (not illustrated). **Post-polio Syndrome:** Distal degeneration of enlarged motor units with denervation of muscle fibers is believed to be the most likely cause of PPS.

In *Current Trends in Post-Poliomyelitis Syndrome* by Daria A. Trojan, MD, and Neil R. Cashman, MD. Copyright 1996, Milestone Medical Communications, a division of Ruder-Finn.

muscle would restart at this high level, and we could show a decline with the stimulation of the whole muscle. Single-fiber EMG demonstrates the phenomenon called jitter, and increased jitter is a measure of dysfunction of terminal axons.

We can also use a stain for a special molecule called neural cell adhesion molecule. When muscle fibers are happy, when they are appropriately and correctly supplied by nerve fibers, they suppress production of this molecule. When they are unhappy, when their nerve fibers are not communicating with them, they express this molecule. We can see staining in 10-15% of the fibers, strongly suggesting that a large proportion of the muscle fibers are unhappy. They are not getting the proper connection with the nerve fiber.

Finally, in a series of experiments done by my colleague, Daria A. Trojan, MD, MSc, we broke down neuromuscular transmission with increasing rates of stimulation, in a technique called stimulation single-fiber EMG. With increasing rates of stimulation, there is increasing jitter indicating a defect in the transmission between the nerve and the muscle.

Thus, we have many lines of evidence to strongly suggest that the terminal axon is dysfunctional. It is not functioning properly on its road to complete degeneration. There is an intervening period of dysfunction, which may last for weeks to years.

Dr. Trojan and I have determined that part of the terminal axon dysfunction is due to a defect in the release of acetylcholine. An increase in acetylcholine may reduce fatigue and fatigueability and may increase strength. In an open drug trial of Mestinon

(pyridostigmine) in 1994, we measured fatigue in people with post-polio syndrome, and found a reduction in fatigue in the people taking Mestinon. In 1997, the North American Post-Polio-myelitis Pyridostigmine Study (NAPPS) found that Mestinon did not provide significant benefits with respect to quality of life, fatigue, or isometric muscle strength compared to a placebo, although a trend was noted

towards increased strength in very weak muscles.

We know there is terminal axonal degeneration. We also believe strongly that there is terminal axonal dysfunction not readily treated. We may be able to support the function of a terminal axon for years or decades, once we know why they are dysfunctional and how we can effect an improvement in this process. ■

RESEARCH FOCUSES ON BARRIERS TO PARTICIPATION

During the next two months, a random sampling of readers of *Polio Network News* will receive a comprehensive mail-in survey regarding lifestyles and activities. International Polio Network did not divulge your name to the researchers, and you will be identified only if you return the survey. However, we do encourage you to participate.

The project, headed by David B. Gray, PhD, in the Program in Occupational Therapy at Washington University School of Medicine in Saint Louis, Missouri, is funded by the Centers for Disease Control and Prevention. The goal of the three-stage research project, "Mobility, Disabilities, Participation and Environment," is to create a practical and useable assessment tool that can measure the effect of environmental factors on the participation of people with mobility limitations.

During the first-stage of the study, polio survivors and spouses from the Saint Louis area participated in interviews and focus groups to describe their activities related to transportation, employment, leisure activities, and home. They discussed what factors prohibited or helped them participate. The researchers, who also sought the opinion of health professionals who work with polio survivors, used the collected information in creating the mail-in survey.

The cross-disability study also includes people living with multiple sclerosis, spinal cord injury, cerebral palsy, stroke, and general mobility limitations.

POST-POLIO DIRECTORY 1999

will be available March 1, 1999. International Polio Network (IPN) will send forms to all clinics, health professionals, and support groups listed in the 1998 edition in early January. Please return the form (noting any changes in the information) to IPN as an indication of your willingness to stay updated on post-polio issues and to be listed as a resource for your geographic area. If you want to be added to this self-identified list, send your name, address, phone, fax, and e-mail to IPN.

Post-Polio Directory 1999 is available for \$5 USA; \$6 Canada, Mexico, and overseas surface; \$7 overseas air (US funds only). (Many readers pay for the *Post-Polio Directory* when they renew their subscription to *Polio Network News*.)

IVUN RESOURCE DIRECTORY

1998/1999, an excellent networking tool for health professionals and both longterm and new ventilator users, will be available in November 1998. Sections include health professionals, ventilator users, equipment and mask manufacturers, service and repair, organizations, etc. The cost is \$5 USA; \$6 Canada, Mexico, and overseas surface; \$7 overseas air (US funds only).