



Rancho Los Amigos

Post-Polio

Support Group

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Current Research in Post-Polio Syndrome

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This report is based on Dr. Perlman's May 15, 2005 presentation to the Post-Polio Support Group of Orange County. It includes information on post-polio research related to more accurate diagnosis, aging with a disability, rehabilitation, other treatments, plus current and proposed research.

First the Bad News

We are dealing with the late effects of the epidemics of the 40s and 50s, but the world is still not polio-free. The World Health Organization's goal of eradicating polio by the end of 2005 probably will not be met.

- In 2003 only six countries still had wild-type polio – Nigeria, Niger, Egypt, Pakistan, Afghanistan, and India (down from 125 countries in 1988).
- The strain of African poliovirus that has spread in northern Nigeria (due to a

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2-year boycott of the vaccine) has now been carried to other African countries, Saudi Arabia, and Indonesia. Those countries had been polio-free for periods of time so they had stopped vaccinating.

- Vaccination programs must continue even if active polio infection is not apparent.
- West Nile virus might become an increasing concern as a mimic of acute poliomyelitis. In one of its manifestations, as it affects the nervous system, it can cause a very polio-like illness. In other countries there are other viruses that can mimic polio.

In June 2005 Rotary International turns 100 years old, with clubs in 168 countries. It has contributed nearly \$600,000,000 over the past 25 years toward vaccination programs to eradicate polio.

Dr. Perlman: Some kind of vaccination program is probably going to have to continue to prevent the re-emergence of polio. Even if active polio infection is not apparent, the risk will still be there. Polio may always be with us, even if all active cases can be eliminated throughout the world.

Some of the things that are learned in polio rehabilitation and post-polio related conditions may still be applied for another generation or two, even after native polio has gone into quiescence.

Do people who had polio need the vaccine?

Yes, because there are three strains of wild polio. Polio survivors had only one strain, so they need to be vaccinated against the other two strains if traveling to a country where there is still native polio. Updating polio and other vaccinations should be discussed with the survivor's general physician.

The Good News

This year's good news is that there was more in the medical literature related to post-polio than last year.

- Post-polio review and education is spreading in the health community. There have been 26 new publications related to post-polio syndrome in the past 12

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months:

- * 4 review articles (in neurological, nursing, and other professional journals)
 - * 14 focused on better diagnostic techniques
 - * 3 were related to rehabilitation
 - * 4 presented other treatments
 - * 1 article questioned whether Frida Kahlo had PPS
- Two abstracts were presented at the April 2005 Neurology meetings compared to none last year.
 - Two new National Institutes of Health (NIH) studies and one new Post-Polio Health International (PHI) study were launched. More information on these appears later in this report.
 - Did Frida Kahlo, the famous Mexican artist, have PPS?
She survived polio at age 6 (residua in her right leg) and a severe bus accident at age 18. “Although Frida’s recovery was miraculous (she regained her ability to walk), she did have relapses of tremendous pain and fatigue all throughout her life, which caused her to be hospitalized for long periods, bedridden at times, and also caused her to undergo numerous operations. She once joked that she held the record for the most operations. Frida underwent about 30 in her lifetime. She also turned to alcohol, drugs, and cigarettes to ease the pain of her physical suffering.”

Taking the Pulse of New Research

1. More Accurate Diagnosis

Dr. Perlman: These four articles focused on better ways to make a more accurate diagnosis of post-polio and to follow the changes. Why is this a concern? One of the great needs in polio research is to have a standard way to measure change. If a polio survivor is getting worse, how much worse is he getting? How can the changes be measured so that the doctors in other research centers can measure change in exactly the same way and compare results? When polio decline can be measured in consistent ways, then polio improvement can also be measured.

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- Horemans HL et al. 2004; *Arch Phys Med Rehabil.* 85:1929-32 reported on two walking tests (distance walked in 2 minutes at self-preferred speed; time to walk 75 meters at maximal speed) showed good test-retest reliability and could detect change as small as 15%.

Dr. Perlman: Good test-retest reliability means that if the test is given one day, then again another day, and again another week or two later (even with different examiners), the results would be basically the same, unless there was a major change in between, such as illness, injury, or being placed on a treatment that helped. Detecting change as small as 15% is good; this probably indicates a real change that must now be discovered.

- Finch LE et al. 2004; *Am J Phys Med Rehabil.* 83:613-23 reported that use of a standardized treadmill protocol also showed good test-retest reliability, intra-rater reliability, and inter-rater reliability.

Dr. Perlman: Individuals were put on a treadmill with a standardized protocol, certain speeds and certain resistance, had them do it one week, again the next week, had different people run the testing, and found good test-retest reliability. If the protocol was followed, the results were about the same, regardless of who was conducting the test. This might also be a reliable way to test performance in a polio survivor with walking-related issues who is starting a new treatment. That treatment could be a rehab treatment or a new drug. Use of a standardized treadmill protocol is something that may be considered for future drug trials.

- Allen GM et al. 2004; *Muscle Nerve* 30:1722-81 reported impaired EMG-related muscle endurance with sub-maximal exercise in the upper limb correlated with subjective new weakness and recent decline in Activities of Daily Living (ADLs).

Dr. Perlman: This EMG study looked at exercise (arm) that was not pushed to the point of fatigue. They were able to look at electrical changes before, during, and after exercise, similar to what has been done at Rancho Los Amigos under Dr. Perry. However, these investigators were able to make a correlation between the complaints the individual had about that arm regarding new weakness and changes in the electrical study. This is important because it is known that EMG exams can show old polio and other neurologic diseases that might mimic post-

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polio but EMG studies have not been very good at measuring change. This particular protocol did show a correlation with the changes the patient noticed; the statistics on it showed whether treatment worked or didn't work.

- Prokhorenko EH et al. 2005 presented this abstract at the American Academy of Neurology meetings in April 2005, reporting that the Fatigue Severity Scale is more accurate than other fatigue scales in assessing disabling fatigue in PPS.

Dr. Perlman: Three or four different fatigue scales were compared and the "Fatigue Severity Scale" seemed to be more accurate and covered more types of fatigue that a polio survivor would be experiencing. This sets the stage for the "Fatigue Severity Scale" to be used in future research regarding treatments for fatigue in post-polio.

In order to get grant money for a research project, the researchers have to be able to show the funding agency that they are going to be able to measure what is being tested and can name a protocol that is stable, is sensitive enough to measure change, and that has been proven to work. The fact that this research has been published should make it easier to get research grants funded.

More Accurate Diagnosis – Health Systems

Dr. Perlman: The health insurance climate and other factors can act as barriers to getting proper health care. One huge barrier in health systems is disability.

How do you convince an insurance company or Social Security that post-polio symptoms, as you are experiencing them, are disabling enough to qualify? There is some interest in getting information in the literature and getting health systems in general ready to record proper information. If a person's medical record reflects the truth about his polio symptoms, it is going to be easier to access care and also to access disability factors if needed.

Quality of life is now felt to be an important measure in chronic illnesses, including post-polio. Part of that illness is not just how strong a muscle might be, but how the quality of life is impacted by that condition. Two articles address this:

- Stuijbergen AK et al. 2005; *Soc Sci Med.* 60:3383-93 reported a study of 1600

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polio survivors, which revealed that quality of life measures are the outcome of complex interactions of severity of impairment, resources/self-efficacy/acceptance, and health promoting behaviors.

Dr. Perlman: Quality of life measures are important in tracking the stages of an illness. They are determined by interactions of the severity of the original polio and its residua, resources that were or were not available, the person's own "get-up-and-go" (of which most polio survivors have plenty), accepting post-polio changes and being willing to work with them (instead of pretending that nothing is happening), and adapting health promoting behaviors.

Examples of health promoting behaviors are seeking out proper bracing, making dietary changes if weight is an issue, finding a physical therapy regimen that would improve endurance, reduce fatigueability but not exhaust them - even if they had to see two or three physical therapists until they actually found the right one, etc.

The major factors impacting the quality of life for people with more severe disabilities are being able to recognize what is needed and having the resources available to seek it. Somebody with more severe disability, no resources or access to them, depression, and other things that kept them from seeking proper care, had poorer quality of life.

This kind of research information can be used in promoting the development of more multi-disciplinary centers and promoting funding from insurance. These types of multi-disciplinary interactions will greatly improve quality of life, which is a key measure now.

- Bouza C et al. 2005; *Health Policy* 71-1106 reported that more accurate diagnostic templates (Manual Muscle Testing, Activities of Daily Living, Quality of Life) for PPS will provide useful guidelines to health professionals and policy makers for the provision of necessary health-care measures and appropriate resources.

Dr. Perlman: Manual Muscle Testing is a standard technique that really should be done by everybody. Anyone visiting a muscle specialist, a neurologist, even a general internist, certainly a physical therapist, should have manual muscle testing

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done. This is the standardized way to test individual muscles. It is part of the picture, but not the whole picture.

Standardizing of motor function testing, standardizing questions, and recording activities of daily living and quality of life will provide useful guidelines to other health professionals, people who make health care policy and insurance policy so that adequate resources can be provided.

More Accurate Diagnosis – Aging With a Disability

- Kalpakjian CZ et al. 2005; *Menopause* 12:78-87 (from PHI study of 2003) reported that menopause symptom scales that standardized on non-disabled women should be used cautiously on women with physical disabilities.

Dr. Perlman: Non-disabled women experience menopausal symptoms differently and report them differently than disabled women. A scale that would guide a physician to offer treatment for menopausal symptoms in a non-disabled woman may not be as sensitive in somebody with a disability.

- Smeltzer and Zimmerman 2005; *Orthop Nurs.* 24: 33-9 reported that the Simple Calculated Osteoporosis Risk Estimation (SCORE) is not accurate in women with disabilities.

Dr. Perlman: High risk for osteoporosis almost guarantees that a person will get a bone density study; low risk for osteoporosis in the HMO environment probably will not offer a bone density study. It is known that polio survivors with weakness in muscles do have a greater risk for thinning of the bone and a greater risk of fractures because of that.

On this SCORE scale, which is the standard one used in the general community, it was not accurate in women with disabilities. It did not ask the right questions and it did not measure the right things.

So the more accurate we are and the more we hold our physicians to these standards of care, the better the long-term outlook is going to be.

2. Rehabilitation

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There are two excellent review articles on rehabilitation.

- Jubelt B 2004 Mar; *Current Treatment Options in Neurology* 6(2):87-93

Dr. Perlman: This is an excellent review by Dr. Jubelt. In detail he stressed the use of non-fatiguing exercise (including upper body exercise machines and pool therapy for cardio), energy conservation and pacing, weight loss, bracing and other assistive devices, swallowing and speech therapy, treatment for sleep, breathing, or pain related issues and appropriate use of anti-inflammatory agents and other medications. (The Vioxx story was breaking about this time; Celebrex is now used cautiously in small doses as well as drugs in the Motrin family.)

[Celebrex is a COX-2 Selective Non-steroidal Anti-inflammatory drug (NSAID).

For more information visit the FDA website:

<http://www.fda.gov/cder/drug/infopage/COX2/default.htm>.]

- Trojan and Cashman 2005; *Muscle Nerve* 31:6-19

Dr. Perlman: This is a similar, more recent review by well-known polio researchers in Canada emphasizing very similar things.

The word is getting out. These interventions should be standard of care. For example, even if a polio patient is not having swallowing problems, the doctor needs to ask the patient. If the doctor does not ask, it is a concern (even if the doctor thinks the patient did not have bulbar polio and the swallowing is not a problem). When a polio survivor sees his doctor for an annual physical, these things should be brought up.

Symptomatic Treatment - New drugs

There are four types of post-polio pain described by Dr. Anne Gawne: nerve pain, overuse pain, sprain and strain pain, and orthopedic pain. There are two new drugs for use in “nerve pain”, Cymbalta and (soon to be released) Lyrica.

Cymbalta is in the same family as Prozac (a selective serotonin reuptake inhibitor) and closely related to Effexor. Cymbalta is the first one that has been tested and licensed for neuropathic pain. So if a person’s doctor has ordered an anti-

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depressant drug for pain and/or depression or fatigue, and it is not working, there is something new that could be tried.

Lyrica is licensed for treatment of epilepsy (similar to Neurontin which is also used for neuropathic pain). It is a calcium channel blocker that the FDA has indicated for pain also.

There is continuing development of drugs for pain and also for fatigue. The drugs for fatigue are coming out as treatments for sleep disorders but could also be tried for fatigue. Provigil is out now and several others are in development.

3. Other Treatments

Dr. Perlman: Three or four years ago I spoke about exciting research that was just being published by a Swedish group headed by Gonzalez regarding the role of the immune system in post-polio. We know that aging increases the risk of a polio survivor developing new weakness and new fatigueability with secondary pain. One of the thoughts is that it is an aging process of those recovered nerves – they recovered from the acute polio, they were a little more fragile, and they are not going to age as well. I think this is the standard approach now to post-polio and its underlying cause.

However, Dr. Dalakas of the NIH and others have found evidence of activation of the immune system - there are immune chemicals that have been found in the spinal fluid and immune cells that have been found around the spinal nerves and in muscle that could be causing inflammation and could be contributing to symptoms of post-polio. The immune system has many facets and maybe only one or two of them could be targeting post-polio.

The Gonzalez group actually found several new chemicals elevated in the spinal fluid of polio survivors. They were elevated way beyond what they should be in an average person - to a level that is seen in other neurologic diseases where the immune system is involved. The researchers thought that perhaps these chemicals could be measured to show activity of post-polio and then develop a treatment for post-polio. That was three years ago.

Below is the most recent publication from this group.

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- Gonzalez H et al. 2004; *Neuroimmunol.* 150: 139-44 presented information on treatment with IVIG (intravenous immunoglobulin).

Dr. Perlman: If a person has an over-active immune system that is making antibodies targeting a muscle, nerves, liver, joints, or any area of the body that shouldn't be inflamed, a large infusion of generic gamma globulin can go in there and root out the bad antibodies thereby taking the inflammatory stress off that area.

These researchers used IVIG with a small number of polio survivors and measured the inflammatory chemicals in blood and spinal fluid before and after treatment. They found that the treatment reduced the levels of some of the inflammatory chemicals. Six were found and two were specifically reduced: IFN-gamma and TNF-alpha. These two may be the ones that are most likely to respond to this type of treatment. In this short trial they were not able to determine if this actually helped the symptoms of the individuals. They want to continue this research with a long-term trial to see if symptoms actually improve by reduction of those two chemicals.

IVIG is expensive, so in order to get approval from insurance companies, it must be shown to be effective.

- Farbu E et.al. 2004; *Tidsskr Nor Laegeforen* (a Norwegian journal) 124:2357 reported on a case where one woman with PPS was treated with IVIG in a serial fashion and she actually did have improved strength and reduced fatigue.

4. Current Research Studies

- Polio-Polio Health International recently awarded a \$25,000 research grant to a team at Johns Hopkins to study the early use of non-invasive positive pressure ventilation (NIPPV) to prolong survival in patients with ALS and possibly other neuromuscular diseases (PPS).

Dr. Perlman: In a way, these positive pressure ventilators are like internal bracing for the breathing system because they give a little boost to inspiration so the breathing muscles don't get as fatigued.

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Pilot studies of the use of NIPPV in chronic respiratory failure suggest that it prolongs survival. It is not clear whether this is disease modifying or just symptomatic for late-stage problems. In polio, if a leg is braced, the strength of the braced muscles can improve; so the same thing could possibly happen here.

- The National Institutes of Health will study the use of Provigil (modafinil) to treat fatigue in PPS.

Dr. Perlman: Provigil is licensed for the treatment of excessive daytime sleepiness. They will see if this drug can reliably improve fatigue and give people with PPS stable energy levels. For information 1-800-411-1222.

- The NIH will study brain physiology in polio survivors.

Dr. Perlman: This study will use transcranial magnetic stimulation. (Many people are familiar with transcutaneous nerve stimulation (TENS) - in which a nerve or a muscle trigger point is electrically stimulated to reduce pain.) In this study magnetic waves through the skull will be used to directly stimulate motor nerves.

Until now transcranial magnetic stimulation has been used for diagnosing a variety of motor nerve problems. This is a way to stimulate the nerves, measure their response, and learn if the nerve is affected by the disease and how severely.

In polio there are a lot of unexplained factors related to fatigue: central fatigue and brain fatigue especially, which are not well explained. One possibility is that polio caused subclinical damage to the motor cortex. This group wants to look at how easily they can stimulate the motor nerves in the brain, which connect to the motor nerves in the spine, which then connect to the muscles. Motor nerves in the brain may also have had polio involvement. Polio wasn't just a spinal disease; it was really a disease of the entire brain. Many people who had total brain involvement probably did not survive the acute attack.

Subtle ways have been found to measure central changes as reflected in Dr. Bruno's reports about MRI scans and reports by others showing central change that might relate to central fatigue and other central factors. Autopsies in some polio patients have found damage to the brainstem and motor cortex as well as to

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spinal motor neurons.*

This NIH group will be looking at magnetic stimulation in the central motor pathways to see if those motor pathways never recovered well and are operating at a lower level, or perhaps they set up different connections, like the peripheral connections to the muscle did. If a muscle could be looked at under a microscope it might look normal on the surface, but what is going on with the neural attachments underneath could be quite different – they might be giving a good response but the wiring could be really changed.

The same could be going on in the brain. This group is trying to demonstrate that if there are changes in the brain, they might be able to predict who would be most likely to develop post-polio symptoms affecting central fatigue or other aspects of motor function.

Risk factors for PPS that are currently known include aging, severity of the original polio, level of best recovery, activity levels (the presence of overuse) but there may be other factors that could be looked at with simple testing.

Proposed Research Studies

- The drug Riluzole protects nerves from nerve death. It is licensed for use in Lou Gehrig's disease (ALS).

Dr. Perlman: In ALS there is a domino-like effect where nerve cells die. Some people have thought that whatever is stressing polio nerves might also be leading to nerve cell death. So perhaps drugs in this family could be used to protect those nerves and strengthen them so they could resist other stressing that is occurring. A small study on this may be announced.

- DHEA or testosterone supplements for post-menopausal female polio survivors with low androgen levels and PPS

Dr. Perlman: Here in Southern California there is a group of physicians who are probably going to be looking at these testosterone supplements. During menopause estrogen and androgen levels decline. Low androgen levels are associated with weakness. Women with low androgen levels from a variety of

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conditions can have improved strength after being placed on low amounts of testosterone. So there is some interest in this study that is going to be designed by an endocrinologist or a gynecologist with the help of several other physicians.

They will look at testosterone in a way that might get it licensed as a treatment for post-polio. Can strength be improved without the side effects of testosterone (virilization [masculinization], liver damage, etc.) on both men and women? Testosterone is not a totally benign treatment; but if testosterone would be a way to conserve and improve muscle strength and prevent that one percent per year decline, it would certainly be worthwhile investigating.

Resources:

www.post-polio.org

www.ncbi.nlm.nih.gov/entrez (PubMed) (Search “post-polio”)

www.clinicaltrials.gov (Find active studies)

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