Research

Summary of Research Presentations from Strategies for Living Well, June 2005

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Who is likely to report a diagnosis of post-polio syndrome?

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In 1994 and 1995, the National Health Interview Survey identified and questioned a national sample of polio survivors—not just survivors seeking medical attention or associated with support groups. Based on the number of respondents, it is estimated that 920,000 polio survivors were living in the United States at that time. The survivors were asked a series of questions about their past and current health, including whether they had been diagnosed with post-polio syndrome (PPS).

- 25% reported they believed that they had PPS, while only 11% reported that they had been diagnosed by a physician. *(Note: Today, 11 years later, more survivors and more doctors know more about post-polio syndrome.)*
- Survivors who had polio as an adult were three times more likely to report PPS than those who had contracted polio during their childhood. This may be due, in part, to these survivors' current age. They may have better access to regular medical care because of their Medicare coverage, and therefore, be more likely to receive a timely diagnosis.
- No relationship was found between the length of time of the respondents' polio infection and the time of the survey and the likelihood that they reported a diagnosis of PPS.
- There was no difference in the rates of diagnosis of PPS in men versus women. Since the vast majority of respondents were white, it was not possible to tell statistically if there were differences in rates by racial or ethnic group.
- Respondents whose polio infection was more severe (for example, those who had more than five muscle groups affected, or those who required hospitalization for their original treatment) were more likely to report a diagnosis of PPS.
- Respondents were asked a series of questions about their view of life, similar to Type A personality questions that have been used in other surveys. Respondents who scored higher on the answers to these questions had a slightly *lower* likelihood of reporting a diagnosis of PPS.
- Future research on PPS needs to be expanded to include all polio survivors, with a special effort to include those who are not European-Americans. They may not have received an accurate polio diagnosis or standard treatment for their polio at the time of the epidemics due to the segregation that existed in the health care system in the US at that time.
- Future research should also identify what factors—*not just physical factors*—put polio survivors at risk of developing post-polio syndrome. ▲

Mouse Model of Post-Polio Syndrome for Growth Factor Therapy

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A "polio mouse" has been developed with hopes to find a therapeutic intervention for post-polio syndrome (PPS). The infected mice react to the polio attack much the way humans do. In SUNY's study,

- 49% died,
- 9% had no paralysis,
- 42% survived with paralysis, and
- None had residual inflammation or viral infection with the continued motor neuron deterioration.

One year later, the equivalent of 30 to 40 human years, 50% of the surviving mice developed late weakness.

There has been some study of people with PPS taking growth factors. However, no useful information resulted for a couple of reasons.

- The dosages were too low and not repeated often enough.
- The growth factors were injected under the skin or into a muscle and did not reach the motor neurons.

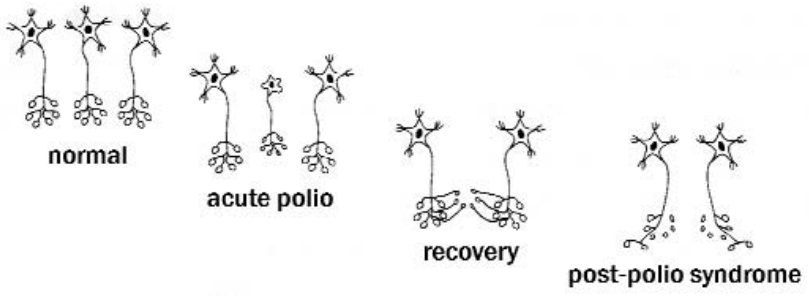
The newer research intends to use two types of growth factors on the "polio mice:"

- GDNF: Glial cell lined-derived neurotropic factor. Its purpose is to maintain the health of the motor neuron cell body.
- IGF-1: Insulin-like growth factor. Its purpose is to strengthen and maintain the motor neuron sprouts.
- A combination of these two factors is intended to stop the late weakness of polio.

In order to deliver the growth factor precisely to the motor neuron cell body and sprouts, the researchers will use a benign virus vector which does not damage the nerve cells. The virus vector carrying genes of the two growth factors will attach inside the motor neuron and replicate. It is projected that the injection of additional virus vectors will only have to be done every six to nine months.

If this procedure is successful with mice, the next step will be to try it with polio survivors. ▲

Pathophysiology of Post-Poliomyelitis Syndrome



Normal: Three normal motor units are presented.

Acute Polio: Invasion of one motor neuron by poliovirus produces degeneration of the affected motor neuorn 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.

SOURCE: Trojan, D. & Cashman, N. *Current Trends in Post-Poliomyelitis Syndrome,* 1996.

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Study Using Modafinil to Treat Fatigue

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Post-polio fatigue is not simply muscular or physical. It involves emotional, intellectual, social and other related functioning.

Modafinil (Provigil®) has been successful in treating fatigue in patients with other neurological disorders, including multiple sclerosis.

First Study: The PPS program sponsored by the Uniformed Services University enrolled (June 2005) volunteer polio survivors to test if modafinil can reduce fatigue in polio survivors experiencing PPS. The results of this randomized controlled trial showed that modafinil was not superior to placebo in alleviating the fatigue.

Second Study: The program has enrolled polio survivors to look at alterations in their brains and spinal cords in order to explain the development and the origin of PPS symptoms. This is not a drug treatment trial. Electrophysiology and magnetic resonance will be used to map possible residual abnormalities in the central nervous system caused by the poliovirus during the original infection.

Third Study: We also will look at cognitive problems that are common among polio survivors who have PPS. The study will measure the brain's ability to concentrate, sustain attention, register and memorize information with the use of traditional neuropsychological tests. Recruitment for this study is expected to start in May of 2006. Polio survivors with and without PPS are needed for this study. Any polio survivor is welcome to enroll, but funding is not available for transportation to the site. ▲

Understanding Research

After every international conference, PHI is asked, "What's the latest research?" Thanks to polio survivor Baldwin Keenan, this issues features the summaries of four presentations (pp. 4-7). Three of the researchers discussed pharmacological possibilities—modafinil, GDNF and IGF-1 and intravenous immunoglobulin (Ivlg). The next question is, "Should I, as a polio survivor, try it?"

The findings in the modafinil study were that it did not alleviate fatigue, which is the same conclusion as that of a team of researchers from the University of Alberta, Canada. K.M. Chan and colleagues reported their study in the January 2006 *Muscle & Nerve* [33(1):138-41].

GDNF and IGF-1 are just now being tested on mice. There is no decision to be made.

By all accounts, intravenous immunoglobulin (Ivlg) sounds promising. But, there are many questions. Is the research "good" research? Which polio survivors would it benefit? All of us? A select few? What are the side-effects? These and other questions will be answered in the next issue of *Post-Polio Health* by Lauro S. Halstead, MD, National Rehabilitation Hospital, Washington, DC, and Julie K. Silver, MD, International Rehabilitation Center for Polio, Framingham, Massachusetts. ▲

Cytokines are small secreted proteins which mediate and regulate immunity, inflammation and hematopoiesis (the development of blood cells).

Intravenous Immunoglobulin Treatment for Improving Muscle Strength

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Post-Polio Syndrome, described as weakness and atrophy in skeletal muscles, occurs when there is a failure in capacity of a nerve cell body to maintain large motor units. The large motor units are supported when the capacity for re-innervation is greater than denervation. Eventually this mechanism reaches an upper limit leading to muscle weakness. The cause of the denervation is unknown at the moment.

An ongoing inflammatory process in the central nervous systems of post-polio patients has been described in some studies, but has not been found in other studies.

Our study in 2002 found an increase of cytokine production in the central nervous system of post-polio patients.

We know that:

- Cytokine levels are greater when there is an inflammation.
- Cytokine levels are higher in people with multiple sclerosis (MS), a known neuroinflammatory disorder.
- The level of the increase in the post-polio patients was almost the same as in the MS patients.

We checked older studies to see what work had been done.

- Dinsmore reported an effect of prednisone in high doses and the effect eroded as the doses were lowered.
- Ann Bailey, MD, at Warm Springs, Georgia, in the early '80s, treated 80 patients with the oral vaccination, and 50 of those patients reported a positive effect on their symptoms.*

Due to her results and to the pattern of the cytokine increase, we began an open, uncontrolled study using intravenous immunoglobulin (IvIg) in 16 post-polio patients.

We were able to down modulate the cytokines, but what is the gain for the patient? We next developed a multicenter placebo-controlled study, double-blinded in 135 post-polio patients. (In the former study, we used 90 grams of IvIg; 30 grams daily for 3 days.)

In this study, we used 30 grams for 3 days, repeated twice. We noted an increase of muscle strength of 4.3% in the post-polio patients. In the placebo group, muscle strength was decreased by 5.7%. This was statistically significant. The *natural course* of decrease in strength was 5.7% in one-half year.

The benefit: Post-polio patients selected for the study had an increase in cytokine levels, indicating inflammation in the central nervous system. The inflammation was down-modulated by the intravenous immunoglobulin (IvIg) and down-modulated inflammation led to increased muscle strength and should result in a better quality of life. ▲

**Using oral polio vaccine to treat PPS is not an accepted practice.*

References

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