PHI’s Fourth Research Award Final Report

Regulatory T Cells as a Biomarker of Post-Polio Syndrome

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There are large numbers of polio survivors today who contracted acute paralytic poliomyelitis prior to the advent of widespread vaccination programs against poliovirus (PV). What is under-appreciated is the fact that polio survivors are many years later at risk of developing new neurological deterioration, a condition recognized in the late ’80s as post-polioymelitis syndrome (PPS). PPS is a slowly progressive disease in individuals previously affected by paralytic poliomyelitis that is characterized primarily by new muscle weakness and atrophy.

Diagnosis of PPS is time-consuming and complicated by the need to rule out other diseases that could explain the new symptoms. The ability of a physician to diagnose a specific disease can be significantly aided by the availability of one or several disease biological markers (termed biomarkers). No biomarker(s) has (have) been identified for PPS as yet that could assist in providing a definitive, easy and rapid diagnosis.

In this study we had three groups of individuals – (1) healthy individuals who never had disease associated with poliovirus and were vaccinated with the polio vaccine, (2) stable polio survivors, who suffered from poliomyelitis and may have had the vaccine but currently do not have symptoms associated with PPS, and (3) individuals with PPS. We recruited 28 individuals during the one-year period of this study, which included 12 healthy and 12 PPS individuals.

Disease biomarkers are measures of biological parameters indicative of a disease process. They are useful because they can assist in diagnosis or provide a means of monitoring the disease as it progresses and the effectiveness of different therapies. The study conducted at the University of Arkansas for Medical Sciences (UAMS) was, therefore, designed to answer a simple question: Are there signs or changes in the immune system (that is an immunological signature) that can be linked to post-polio syndrome (PPS)? If so, these changes in the immune system could be potentially used as a biomarker to diagnose PPS quickly and efficiently and to possibly provide clues as to the causes of PPS.

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Rahnuma Wahid, PhD, not only explains the results of the study funded by PHI’s Research Fund, but also gives us a basic lesson in immunology. Rahnuma often visits family in Bangladesh where a few cases of paralytic polio were reported even in 2000 and 2001.

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**How I Learned to Stop Worrying and Love Technology**
Daniel J. Wilson, PhD, reminds us we are not alone, that others may not see us as we see ourselves and reaffirms the idea that in looking “more disabled” we can be more active and involved.

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Improved technology has improved PHI’s ability to connect with survivors around the world. T.V. Ganesh expresses his desire for more awareness of post-polio problems in India – WE’RE STILL HERE! (See page 12).

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Thank you for your responses to “To Have Surgery or Not to Have Surgery – That Is the Question!” by Debbie Hardy. The recommended surgeons are listed.

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With thanks, we publicly acknowledge our major supporters. There is a trend of people becoming PHI Members “because a polio survivor (or my physician) said I should join.” Thank you for the endorsements!

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SAVE THE DATES ...
WE’RE STILL HERE! and Living with Polio in the 21st Century are scheduled.

Joan L. Headley, Executive Director of PHI

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**How to contact PHI**

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However, the number of stable polio individuals interested in participating in the study was much lower than we had anticipated. We were only able to recruit four stable polio survivors.

Our strategy was to study the cells present in the blood. We wanted to see whether the types of immune cells seen in individuals with PPS were different from those from healthy individuals or individuals with stable polio. Blood contains B cells and T cells. These cells are major components of the immune system in humans. B cells produce antibodies that protect from diseases caused by viruses or bacteria.

The polio vaccine, for example, causes the body’s B cells to make antibodies that specifically recognize and kill poliovirus and thus, can protect the vaccinated individual from being infected by the virus. The T cells can recognize cells that are infected by a specific virus and kill these sick cells. Poliovirus-specific T cells will kill poliovirus infected cells of the body to protect the rest of the cells in the body from getting infected.

T cells which kill infected cells are known as effector T cells. The functions of effector T cells are controlled by another group of T cells that are called regulatory T cells. The regulatory T cells ‘manage’ the effector T cells and provide restrictions on the effector T cells, so that they do not indiscriminately continue to kill cells.

The regulatory cells are usually present in very low numbers in the blood. However, during infection or other situations where there is inflammation/injury in the body, the number of the regulatory T cells can increase dramatically in the blood. Thus, the number of regulatory T cells present in the blood can provide clues about whether something is different or unusual in the individual.

Each of the individuals who participated in the study donated blood. To determine whether there is evidence of an immune biomarker in polio survivors, we examined blood donated by each of the individuals to determine whether:

(i) unusual levels of PV-specific antibodies are present in individuals with PPS;
(ii) higher numbers of the regulatory T cell type are only present in the blood of individuals with PPS; and
(iii) increased regulatory T cells are a signature of past poliomyelitis (that is present in stable polio survivors as well as PPS).

To date no one has used this approach to study PPS. Therefore, it was important first to just measure the levels of poliovirus antibodies and regulatory T cells in the blood of PPS and healthy individuals. When the results are grouped according to whether the person has PPS or is healthy, the type of data that one might expect is shown in Figure 1. Each circle represents the number of regulatory T cells or level of antibody measured in a person.
The healthy individuals would have similar but low levels of antibodies and regulatory T cells, while the PPS individuals would have higher levels of these markers. Ideally, the levels of polio-recognizing antibodies or regulatory T cells could be potentially used to help diagnose PPS, if we could see a large difference in the antibody and regulatory T cell levels when groups of PPS individuals are compared with healthy individuals. That is, the differences between groups of PPS and healthy individuals were more like what is seen in A rather than B (Figure 1). If such differences were consistently seen after many healthy and PPS individuals have been tested, then it would be possible to say that high levels of antibodies and regulatory T cells are linked with PPS.

But, there is still a potential problem with using these immune properties to help diagnose PPS. This is because the blood from polio survivors who are stable needs to be studied as well (see Figure 2). If the stable polio survivors have levels of antibodies and regulatory T cells similar to that of healthy individuals (as drawn in Figure 2A), then we would be more certain that high levels of these biological markers are specifically associated with PPS and these markers could potentially be used as tests for PPS. But if the data from the stable polio survivors are similar to that of the PPS subjects (Figure 2B), then it would suggest that the levels of antibodies and regulatory T cells are indicators of a person who has a medical history of poliomyelitis, as both groups of polio survivors have high levels of antibodies and regulatory T cells. In this case, polio-specific antibodies and regulatory T cells cannot be used as biomarkers of PPS.

Figure 2C shows another possible outcome of the results. If a large number of stable polio survivors could be studied, it is entirely possible that some individuals would have high levels of antibodies and regulatory T cells in their blood, while some would have low levels. Such a range of results could mean that people with high levels of these biological components are at risk of developing PPS, while those who have low levels are not at risk of developing PPS.

Figure 2: Idealized data to show the possible outcomes of a study of polio survivors. A. Graph to show that stable polio survivors (SP) may have levels of regulatory T cells and antibodies similar to levels in healthy individuals. B. Graph to show that SP individuals may have levels of regulatory T cells and antibodies at levels similar to PPS individuals. C. Graph to show that SP individuals may have a wide range of levels of regulatory T cells and antibodies that overlap levels from PPS and HV individuals.
Figure 3 shows the range of results obtained from the study at UAMS of 12 healthy and PPS individuals and the 4 stable polio individuals. The top of the box indicated for each of the three groups shows the highest level of regulatory T cells obtained from the individuals and the bottom of the box indicates the lowest. The line in the center marks the average number for each group.

Our data suggests that PPS individuals have higher levels of antibodies and regulatory T cells circulating in their blood than healthy age-matched individuals, while SP individuals have variable levels of these immune components, which overlap with both the PPS and the healthy individuals.

The cause for the increased levels of these immune components is currently unknown. Importantly, however, the lack of sufficient data from SP donors makes it difficult to make definitive conclusions regarding the role of regulatory T cells (and/or antibodies) as an easily available diagnostic marker for PPS.

**It is important to remember that this is a very small study.** We do not have enough SP donors, to make a final conclusion about whether the regulatory T cells can be used to diagnose only PPS. However, in a larger study: if there are sufficient numbers of SP donors, and they do not have high levels of this cell type but PPS individuals do have high levels, then:

- The target may be used as biomarker of PPS for faster, definitive diagnosis.
- The target T cells may provide clues about what leads to the development of PPS.

The observations from this study suggest that there is some kind of problem with the immune responses in polio survivors, which could contribute to PPS. Whether immune components have a direct role in the initiation and progression of PPS or merely indicate the presence of a problem with the immune system in these individuals is unclear at this time.

**Update on the Fifth Award**

PHI’s Review Panel is currently evaluating eight proposals submitted to vie for $25,000 to be given for Year 2009.

Contributions may be made specifically to The Research Fund. Individuals wanting to remember The Research Fund in their wills should contact PHI’s Board of Director’s representative Lawrence Becker, PhD (lcbecker@bookwork.net) or Joan L. Headley at director@post-polio.org or 314-534-0475.
I have now been struggling with the effects of polio for nearly twenty years. These first appeared as a weakness in my right leg, the one most affected by polio, in 1987. Over the ensuing two decades, the leg got weaker, and I began to have breathing problems at night. The physical problems have led to an increasing reliance on technology to help me breathe at night and to move around during the day. I began using a BiPAP® in the fall of 2000, and since August 2006 I have used both a scooter outside my home and stair glides in the house.

Like some other polio survivors, I resisted getting the breathing machine, the scooter and the stair glides. I was proud of my ability to get around on my own without assistance. I could never walk very far – no Appalachian Trail or marching band for me – but I got around quite easily. I associated assistive devices with disability, and I didn’t consider myself disabled. Inconvenienced at times, but not disabled. Using the technology of assistive devices was something I resisted. I wanted to do it my way, even if that was increasingly painful.

My first concession to the encroaching post-polio syndrome was the BiPAP®. I had spent part of the summer in the year 2000 at San Francisco State University studying disability and disability history with 25 other scholars, some of whom had disabilities of various types. I not only studied the way in which disability is constructed by society and the ways in which those with impairments are made to feel inferior, I also observed the ways in which my colleagues used their assistive devices to function effectively and easily.

When I returned to my home in Allentown, Pennsylvania, I had a sleep study done, which revealed serious sleep apnea, explaining why I was waking up tired. I wasn’t happy about the doctor’s recommendation of a BiPAP®, but decided to try it. Getting used to the mask was not easy. The first couple of nights I did not get through the whole night with the mask on. By the end of the first week, I began to notice a real difference. I was sleeping through the night. And in the morning I was more wide awake and less tired. I have used it every night since, both here and in Europe, except when we have had a power outage. It goes with me when I travel, and I rely on it to help me get a restful night’s sleep.

In some ways the BiPAP® was easy. No one had to know except my doctor, my wife, Carol, and our dog, Abbey – who thought it was a vacuum machine when I first turned it on and fled the room. Because I used it only at night, it was a hidden technology unless I revealed the secret. Fortunately, Carol and Abbey both adjusted to the noise of the machine.

My next device would be more public – using a walking stick when there was snow on the walks. As my leg weakened, it became problematic to walk on uneven pavement such as that covered by snow and ice. So, about five years ago I began using a
bright red walking stick in winter. It was one I had purchased in the early 1990s in Zermat, Switzerland, which made it easy to delude myself that I was getting ready to scale the Alps. At least it didn't look as if I had purchased it at a medical supply store. For the last two years I have used the stick whenever I have any distance to walk. It has helped give me stability and has prevented several falls. But I was experiencing increasing pain and was walking decreasing distances. I realized I needed to think about getting a scooter. In the summer of 2004 I purchased a Volvo station wagon that was capable of hauling a scooter – but I wasn’t yet ready to get the scooter.

Finally, this past summer I decided it was time to get serious about a scooter and stair glides. I could see I made too many decisions not to do things because of the pain it would cause. I checked with friends in the support group about reliable suppliers as well as with colleagues at the Lehigh Valley Center for Independent Living, where I serve on the board of directors. I was able to try out three different scooters to see what worked best for me and which fit in my station wagon. My wife and I also decided to put in two stair glides. In August both were installed so that I could easily get to the upstairs and to the basement (that way I could help with laundry). I also bought a scooter (a Pride Revo) and had a lift installed in the Volvo, so I could get it in and out easily. I began using these new devices immediately.

I think my biggest anxiety about these new technologies was using the scooter. It’s right out there in public – no possibility of hiding if it was going to be useful. I was apprehensive about using it at Muhlenberg College where I teach, but I had a few weeks before classes started so I could adjust to using it on campus. I need not have worried. My colleagues and the students have been very accepting. Some have been interested in the scooter itself, others have asked about the reasons I use it, but most have simply accepted it as part of the scenery. I decided to be very open about why I need it and don’t really mind the questions.

The scooter has made it much easier and much less painful to get around campus. I no longer have to think “do I really need to go to the library” or “do I really want to go to lunch in the union.” I just get on the scooter and go. My only challenge has been the automatic door openers. The maintenance staff is very good at fixing them, but the doors do seem to stop working all too frequently.

Winter and snow will pose another challenge, but the crews have traditionally done a good job on clearing the walks, so I am optimistic.

In addition to using the scooter at school, I have used it at Wegmans, Target, and the mall at King of Prussia. I took it to Valley Forge Park and the Allentown Art Museum. And I have been walking our dog Abbey with the scooter. For several years our walks had been more of the “stroll and sniff” variety. She adjusted to the scooter very quickly and now enjoys longer and more vigorous walks.

As I got used to the new technologies and discovered that they were liberating in many ways, I began to think about why I, and perhaps others, so
often resist using assistive technologies. After all, there are many other technologies I use without a second thought. I have worn glasses since second grade. This essay is written at the computer while listening to the radio. Technologies all. We use technology to heat and cool our homes and to transport us.

But we resist when the technologies can help us deal with the impairments of post-polio. In part, that is because so much of society still views scooters or wheelchairs as emblems of disability. But if we buy into those social attitudes about assistive devices, we are the ones who become disabled. We are the ones who choose not to go places because it is too tiring or too painful. We are the ones who miss out on things we enjoy if we don’t adopt the available technologies.

Surely, if it is normal for many people to walk around the store talking on their cell phones (one more piece of technology), it is normal for me – or you – to scooter through the same store.

I know I waited too long to get both the scooter and the stair glides, in large part because I didn’t want to admit that I needed them. Polio survivors, and others who need them, will be better off if we can think of assistive technologies as just another modern technology that helps us live better and easier lives. Cell phones make for better and easier communication. Scooters and stair glides make for better and easier mobility.

I am not sure I really love technology (and that includes computers, cell phones, and scooters), but I know that all three have made my life easier. We don’t have to embrace technology, but at least let us use the technologies that improve our lives without fear or trepidation. ▲

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*Wilson* is a member of PHI’s Board of Directors, has authored many articles about the history and the impact of the polio epidemics. His most recent book, *Polio Voices: An Oral History from the American Polio Epidemics and Worldwide Eradication Efforts* (Praeger Publishers) was co-authored with Julie K. Silver and released in 2007.

Wilson’s earlier book, *Living with Polio: The Epidemic and Its Survivors* (The University of Chicago Press, 2005), has been favorably reviewed and widely quoted in later works.

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**Have a personal story to tell about living with the late effects of polio?**

Have the late effects of polio affected a relationship, job or lifestyle? Have you found a solution? Do you have an experience to tell that would benefit others? If so, send your story ideas to editor@post-polio.org.
I am T.V. Ganesh. I was born in Delhi (India) on the 29th of August, 1968. I do not precisely remember the day after moving to Bombay when this baffling poliovirus attacked me, as I was an 11-month-old infant. As narrated to me by my parents, one fine morning I had a very high fever. To bring it down the physician in our area administered me with an injection. The next thing which they remember is that although the fever settled down, both of my lower limbs developed terrible weakness.

My parents took great pains to rehabilitate me with vigorous physiotherapy treatments and electric light treatments at All India Institute of Physical Medicines. I had a harrowing experience as a child with both of my legs braced completely from the hip. I used to walk with crutches. The pelvic bands particularly used to be very painful. I used to stand dejectedly at one corner and watch the Physical Education sessions at school. Slowly but steadily the muscles of my left leg regained strength and movement. Over a period of time, the brace on my left leg was discarded.

Never once did I like the ugly shoes I had to wear. I used to cry and bang things around to show the hatred that I had for those shoes, always dreaming of wearing sports shoes. I was unable to attend the prayer sessions in temples, because in our customs we have to remove our footwear outside the temple before entering it.

My initial dreams to wear normal shoes were realized at the age of 18 after my ankle-stabilization operation.

As an adolescent I started playing cricket with a minimum of footwork, and swimming helped me to relax my leg muscles. Now at 37, I have recently undergone surgery for correcting the alignment of my right ankle, my fourth operation.

Educated in finance and business development, I work for a Forex Firm as branch manager. My job involves a lot of traveling from one corner of Bombay to another, making marketing calls. At the end of the day I am exhausted, despite the fact that while on the calls I take a comfortable mode of transportation.

I am not able to walk continuously at a stretch and while getting down off the staircases my legs tremble and shiver. Because of the late effects of polio I think I will have to reconsider my job profile.

Polio survivors in India need an awareness about the late effects of polio and “the dos and the don’ts.” I think we need an association and centres which can provide insight to the orthopaedic surgeons and physicians regarding our condition. Many are taken by surprise when polio survivors come with complaints such as new muscle pain, muscle tiring and overall physical exhaustion.

The media plays a great role in educating people, and I want to involve them in creating awareness about the late effects of polio and to get the government to provide modern facilities for polio survivors.
Readers Respond

In response to the request accompanying the cover article, “To Have Surgery or Not to Have Surgery - That is the Question!” by Debbie Hardy, in the last issue of Post-Polio Health, PHI Members (Nancy Dubois, Barbara Goldstein, Gladys Kiplinger, Rita McGovern, Stuart G. McLennan, Jr., Rick Paris and Marilyn Spera) recommend the following orthopedic surgeons.

Elise Smith-Hoefer, MD
(arm and hand)
Davis, California
530-771-4000

Michael Pinzur, MD
Adult Orthopaedics & Rehabilitation
(foot and ankle)
Loyola University Health System
Maywood, Illinois
708-216-4993

Jeff Jacobson, MD
Washington Brain and Spine Institute
Bethesda, Maryland
301-718-9611

Paul Paterson, MD
Excelsior Orthopedics
(upper extremity, wrists and arms)
Buffalo, New York
716-250-9999

Phil Stegeman, MD
University Orthopedics
(shoulders)
Buffalo, New York
716-898-3323

Frank P. Cammisa, Jr., MD, FACS
Federico P. Girardi, MD
Andrew A. Sama, MD
Hospital for Special Surgery
New York, New York
212-606-1946

Jeffrey Dulik, DO
(knees, hips, carpal tunnel)
Massillon, Ohio
330-832-2662

Mary Ann Keenan, MD
Helen Horstmann, MD
University of Pennsylvania
Philadelphia, Pennsylvania
215-349-8695
215-662-3340 appts

C. Stuart Pipkin, MD
(spine)
San Antonio, Texas
210-495-9047


NEW BOOKS

Understanding Viruses
University textbook includes post-polio syndrome

Teri Shors, University of Wisconsin at Oshkosh, authored a textbook for a mid-level virology class. Published by Jones and Bartlett Publishers (2009), Chapter 11, “Poliovirus and Other Enteroviruses” is 23 pages of history, clinical features, classification and structure of the virus, transmission, prevention and eradication. Post-polio syndrome is also described.

Love, War & Polio: The Life and Times of Young Bill Porteous

Timothy James Bazzett combines research with original letters, interviews, personal recollections and anecdotes to tell polio survivor Bill Porteous’s story. It is a home-spun history lesson about the nearly forgotten polio plague years and our fathers’ and grandfathers’ war. The appendix lists all the polio patients and staff who spent time at the Army and Naval General Hospital (A&NGH), Hot Springs, Arkansas, in the late 1940s.

NEW REQUEST: Polio survivor, Larry Julius (LJulius600@aol.com) was not at A&NGH and, unlike Mr. Porteus, had polio before he was accepted into the service. For the year of 1969, Larry was an Army artillery forward observer in the jungles of Vietnam assigned to the 1st Air Cavalry infantry. Larry is specifically interested in contacting fellow combat vets who have symptoms of Post-Traumatic Stress Disorder (PTSD) and worsening symptoms of post-polio syndrome.
Special Thanks

Post-Polio Health International thanks the many friends and family members who contributed in support of our mission.

Recent contributions to The Research Fund ...

In Memory of
John Maineau
Lucy Weaver
Clifford E. Rowan

Recent contributions to PHI’s educational, advocacy and networking activities ...

In Honor of
Mark S. Fixley, MD
Lorraine Lovain
Joan L. Headley

In Memory of
Michael Coler
Barbara Price
Marcella Edgington
Louise E. Price
Charles Epstien
Clifford E. Rowan
Joan Elaine Flick
Robert Schiesher
Virginia Love
Lucy Weaver

October 1, 2007 - March 31, 2008
Gini Laurie Advocates ($10,000)
Edouard Foundation
ResMed Corporation*
Helen Ford

Platinum ($5,000)
Clark S. Callahan
Respirronics, Inc.*
Dale Medical Products*
Santa Barbara Foundation*

Gold ($1,000)
Gwen Babcock
Jerome Grady
Francine Falk-Allen
Joan L. Headley
Richard Flickinger
William Wischmeyer

Silver ($500)
Gerald Fowler
Saul J. Morse
Lillian Genskow
Post-Polio Support Group
Frederick M.
(Worth, Illinois)
Maynard, MD
Rowan Helping Ministries

Bronze ($250)
Patience Chrisler
Olive Beaham Lansburgh
John R. Fisk
Janice Flood Nichols
Joseph & Jacqueline
Garger
(Downey, California)
Roger & Marian Gray
Polio Epic
Judith Heumann
(Tucson, Arizona)

(* = IVUN)

REMINDER: The children of polio survivor Gilbert Goldenhersh established the Gilbert Goldenhersh Memorial Tribute Fund to assist polio survivors living in Missouri to live independently. Please contact PHI for more details on how to apply for bracing or custom-made shoes.
SAVE THE DATES!

Post-Polio Health International invites you to participate in the second WE’RE STILL HERE! campaign.
Send your ideas to info@post-polio.org and watch www.post-polio.org and the next issue of Post-Polio Health for details.

Ideas for sessions?
Contact director@post-polio.org or call 314-534-0475.

Location: PHI’s 10th International Conference will be hosted by the Roosevelt Warm Springs Institute for Rehabilitation (RWSIR) in Warm Springs, Georgia. Located 70 miles southwest of Atlanta on 940 acres, RWSIR was founded by Franklin Delano Roosevelt in 1927 and served as its medical and vocational rehabilitation center for polio from the late 1920s to the mid-1950s.
To learn more about its storied past and its current modern facilities and services, visit www.rooseveltrehab.org.

“Hope and the Human Spirit – Overcoming Polio” is the title of a year-long exhibit at the Reno County Museum, Hutchinson, Kansas.
The opening, March 29, 2008, was attended by 200 people. The exhibit was created in partnership with the Central Kansas Polio Survivors Group.
For details:
www.renocomuseum.org
620-662-1184
Open Tuesday-Saturday, 9 am-5 pm

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