INFLAMMATION and PPS

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Post-Polio Syndrome (PPS) has been a recognized condition for more than 25 years, with reports of similar symptoms going back to the 1800's. However, we still do not have a grasp of the underlying cause, or causes, of PPS!

We do not know how many polio survivors will develop PPS; estimates range from 20% to over 80%. We do not know why some polio survivors develop PPS and others do not. There is no diagnostic test and PPS remains a diagnosis arrived at after exclusion of other somewhat similar conditions. We do not understand why there is a lag time between recovery from the acute illness and development of symptoms severe enough to compromise the quality of life.

It seems there is very little that we do understand about PPS. However, if we can discover the underlying cause(s) of PPS; if we can find out what is happening at the cellular and even sub-cellular level, there is promise of being able to answer all of these perplexing issues. There is also promise of being able to treat and possibly even prevent the onset of many perhaps most, PPS symptoms.

Little research has been done on PPS, probably because polio survivors are a dying breed. After world wide eradication of polio, the 'lifespan' of PPS will be equal to that of the youngest living polio survivor. Or will it? Poliomyelitis continues to cause paralysis although now the virus causing the illness is not the polio virus but the West Nile Virus, or enterovirus 71, or one of several Coxsackie viruses.

The nerve damage caused by these viruses is virtually identical to that caused by the polio virus and therefore it is likely that PPS, perhaps by then called Post-Viral Syndrome, will continue to bring new limitations to survivors many years after they thought they had recovered. So it remains important to examine the underlying cause of new muscle weakness, central fatigue, pain, memory and word finding problems and other symptoms that accompany PPS.

Fortunately, current research in other areas holds great promise for explaining what is happening to so many polio survivors. The cause of virtually all PPS symptoms can be explained by one word: inflammation! Front line research in the fields of neurology, immunology, physiology and virology is coming together and the many pieces of the puzzle are being laid upon the table.

A good analogy is to think about a jig-saw puzzle. When you dump a 1000 piece puzzle out of the box, some pieces land right side up, others upside down. There is little hope of assembling the puzzle until you turn all the pieces right side up. The next step is to put all the straight edged pieces in a pile and then assemble the outer edge of the puzzle to give you a general outline. After this it is helpful to group pieces with similar patterns or colors together.

This is approximately where we are today in our understanding of how inflammation is related to almost all chronic diseases; PPS, MS, ALS, CFS, Parkinson's, irritable bowel syndrome,

arteriosclerosis and many, many others. This also gives you some idea of how far we have to go until we have a complete picture! Let's look at the puzzle pieces that seem to belong to PPS.

Inflammation has two major causes; injury (including viral and bacterial infection, cuts, strains, operations, etc.) and psychological stress (including major events such as death of a relative, divorce, and job loss, but also including milder, repetitive stress that is encountered every day).

In a person with PPS, when the body suffers an injury, such as physically overdoing by climbing too many stairs, walking on uneven ground, etc. the first reaction is for the cells in the affected area to release a chemical messenger. This messenger, called a proinflammatory cytokine, tells specialized cells, whose job it is to protect you from invading organisms, to come to the site of the injury. At the same time the proinflammatory cytokines activate resident cells and cells that have migrated to the injury and all of them produce more proinflammatory cyto-kines setting up a cascade of events that will involve the entire body.

Two proinflammatory cytokines, interleu-kin-1 and Tumour Necrosis Factoralpha, are especially important in triggering an acute immune response, the body's first line of defense. The acute immune response involves developing a fever, fatigue, loss of appetite, sleepiness and other symptoms. It goes away within a few days. However, if the injury is repeated often – say if a person with PPS persists in exercising a stressed out muscle – then a chronic immune response will set in. The response to chronic stress involves the entire body including the brain and produces central fatigue, new muscle weakness, problems with short term memory and word finding, irritable bowel syndrome and other symptoms.

Recognize them? Indeed. These are the post-polio syndrome symptoms we are so familiar with. In an effort to keep this article shorter than a textbook on immunology, I have omitted the complex chain of events that takes place in the body between the original stress and the onset of PPS symptoms. There are many, many research papers that amply document what happens in the body after activation of the immune system by proinflammatory cytokines and that eventually results in symptoms identical to those of PPS.

Let's take a brief look at how proinflammatory cytokines may be the underlying cause of new muscle weakness. We begin with acute polio and the death of a large number of nerves whose job was to innervate muscles by telling the muscles to contract or relax and thereby allowing you to move a leg or an arm. If 60% of the nerves leading to a leg or arm died, the limb was paralyzed. When fewer nerves died the result was varying degrees of muscle weakness.

In many people, original paralysis or severe weakness eventually resolved; voluntary movement was restored and you could once again use your arm or leg. The body developed a neat trick to allow this to happen. The surviving nerves were able to send out 'neuronal sprouts' to attach to and innervate muscles that had been orphaned when the nerve originally attached to them died off. Thus the surviving nerves were able to activate not only the muscle that they always innervated, but also surrounding muscles creating something called a "motor unit".

This repair was essentially stable for many years. However 30 or more years after recovery from polio, many people begin experiencing new muscle weak-ness. Often the weakness is in the

'good' arm or leg. This may be due to the fact that the 'good' arm or leg was used more. Clearly something happened to the neuronal sprouts; either they no longer could maintain full time attachment to the motor unit or else they may have died off completely. This caused the appearance of new muscle weakness. Once again, I've simplified this a bit – although the general picture is correct. But this is a description of *what* is happening, not an explanation of *why* it is happening.

Enter proinflammatory cytokines. Remember them? Researchers have well established that proinflammatory cytokines cause cells to release neurotoxic proteins. These neurotoxic proteins can damage or even kill neurons by a number of mechanisms including changing the outer membrane of the nerve cell resulting in cell death or increasing reactive oxygen inside the nerve cell which also leads to cell death. It is probable that the neuronal sprouts, that have served so well for so long, are more fragile and may be the first target of proinflammatory cytokines in the central nervous system.

A very important fact is that nerve death only occurs in an activated immune system. The next question is "Do people with PPS have an activated immune system?" The answer is YES! There have been a number of research papers indicating that polio survivors with PPS symptoms have an activated immune system while polio survivors who do not report PPS symptoms do not have an activated immune system [1].

A very recent research paper [2] looked at cytokines in people with PPS, polio survivors without PPS, people with multiple sclerosis (MS), a well known inflammatory neurological disease, and people who had no neurological problems. They found that people with PPS and MS have proinflammatory cytokines in their central nervous system while polio survivors who do not have PPS and people without neurological problems do NOT have proinflammatory cytokines in their central nervous system.

What might cause the presence of these proinflammatory cytokines in people with PPS? One hypothesis is the presence of very low levels of polio virus RNA hiding in nerve cells. This polio virus RNA is not capable of infecting you or other people, but is capable of triggering the production of proinflammatory cytokines and with that, an underlying state of chronic immune system activation.

Other researchers have demonstrated a clear connection between the presence of proinflammatory cytokines and central fatigue [3]. Psychological stress – the kind that doesn't involve overdoing physically – is perceived in the brain and the brain produces proinflammatory cytokines. This can cause profound fatigue, inability to concentrate and other symptoms [4].

Remember that 1000 piece jigsaw puzzle we have spread out on the table? We are now able to put together some of the same coloured pieces to make small pictures that are part of the larger picture. In the same way, we are piecing together what happens when a person with PPS experiences physical or psychological stress. We start to see small pictures and we can just begin to discern the larger picture coming together.

We are coming to the place where it may be possible to treat PPS symptoms using anti-

inflammatory medications. A very exciting trial, using *intravenous immunoglobulin treatment*, is currently underway in Sweden. Preliminary trials of this treatment in people with PPS have yielded dramatic improvements in fatigue and muscle strength! [5,6]

Other treatments to reduce PPS symptoms may be based upon *traditional anti-inflammatory medicines* such as aspirin, ibuprofen, indomethacin and others.

All treatments would have to be done under the supervision of your doctor, but in the meantime, there are some things you can do that are known to minimize inflammation in the body – and with that you might have a reduction of PPS symptoms.

- *Meditation.* You might try meditation. Yes it works...if you do it consistently.
- *Exercise.* Appropriate exercise, under the guidance of a knowledgeable physiotherapist, will definitely lower inflammatory cytokine levels.
- *Pacing.* Pace yourself and don't overdo. This is easier said than done but if you understand that seriously overusing muscles will start the proinflammatory cascade of events and with that bring on or intensify PPS symptoms, perhaps you will be able to justify resting before you go too far.
- *Weight loss.* Adipose tissue – commonly known as fat – is also a producer of inflammatory cytokines. If you needed a good reason to lose weight, here it is.

Finally there are a few things you can try. *Drinking green tea* encourages weight loss and it has neuroprotective qualities. There are also reports that *undenatured whey protein* may be beneficial. These things are probably not as effective as direct medication to lower proinflammatory cytokine levels, but as we incorporate them into everyday life, they will bring positive benefits.

And let's keep working on that jigsaw puzzle!

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Now retired, Dr. Falconer led a laboratory doing research in virology and molecular biology at The Centre for Food and Animal Research, Agriculture Canada Ottawa, Ontario, from 1993 to 2000.
Educational background:

- Post-doctoral fellow in molecular biology at Massachusetts Institute of Technology (Center for Cancer Research), Cambridge, Mass. USA. 1990-1992.
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Marcia was quarantined with polio at age 7 (1949). She had leg and arm weakness followed by complete recovery. She led an active life: swimming, ice-skating and cross country skiing. PPS symptoms first noticed in 1985, with fatigue and leg weakness becoming severe by 1996. PPS diagnosed in 1998.