Polio Biology II
Post-Polio Syndrome's Elusive Etiology

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> **In science, self-satisfaction is death. Personal self-satisfaction is the death of the scientist. Collective self-satisfaction is the death of the research. It is restlessness, anxiety, dissatisfaction, agony of mind that nourish science.**
> Jacques Monod, 1910-1977, New Scientist, 1976.

Monod is someone to listen to. He and his colleagues gave us the first model explaining how a gene can turn on when it is needed and off when it is not. And so, although I don't need a lot of pushing in the direction of questioning ideas, I do think it is of value to be skeptical, especially when someone gives us an unequivocal answer as to the cause of a complex process like Post-Polio Syndrome.

So, the bells went off the other night when I visited the Web Pages of the National Institutes of Health in the States. I scrolled around until I got to Post-Polio Syndrome. And I found a rather authoritative pronouncement that it was caused by the recovery from polio. That the Syndrome can be completely understood in the loss of regenerated fibers, which compensated for the original damage of disease. And that this regression is the result of overcompensation and years of overwork of the nerves that "carried the day" thirty plus years ago. But why? What actually happens? And, although it sounds very plausible, where is the evidence for this?

Why do some people with a lot of polio damage not experience Post-Polio Syndrome? Do their overworked neurons remain stable for some unknown reason? Why is there new brain pathology (if there is) with Post-Polio Syndrome? And, if there is, do brain neurons just happen to lose connections and die at the same time as motor neurons by coincidence, even though they attach to one another and not to muscle that overwork them? I need a deeper understanding of this. Answering that motor neurons "wear out" begs the question: why, what is the mechanism?

Sometimes when an answer is given, as above, the effect is to stifle further research. If there is to be any deeper understanding, we have to comprehend the mechanics of how neurons "wear out". I'd like to offer some food for thought without endorsing what follows, but rather present it to try to convey how complicated interactions between host (us) and parasite (polio) can be biologically. And, as a consequence of this complexity, how difficult it can be to find an ultimate cause.

Polio virus is very small. It is classified with this in mind: Picornaviridae. The particle itself is composed of two parts: a protein case, called a capsid, and the genetic material inside: Ribonucleic Acid (RNA). The

capsid is made of repeating units called capsomers, and each capsomer (a triangular piece like a part of a soccer ball) is made of protein subunits called protomers. Each protomer is the same. So you put together a polio virus by assembling protomers into capsomers, and capsomers into a twenty sided (icosahedron). The genetic stuff (RNA) is inside. The RNA contains very few genes and is unusually small. Unlike larger DNA viruses, polio has no way of fixing mutations when they happen. This would require a larger genome. And mutations do happen during an infection. What I am saying is that when the genetic material duplicates inside an infected cell there is not always perfect fidelity between the parent molecule and its daughter molecule. Pairing mistakes are made. Considering how small polio virus is there can be a million or more duplications within a single cell. We must conclude that there are plenty of mutant genomes (RNA's) produced during the life cycle of polio virus within a motor neuron.

Now, the presence of mutant RNAs would likely interfere with the proper reproduction of normal genomes. First of all, viral genes shut down the cell's normal functions, selfishly requisitioning these materials for its own reproduction. We can assume that there would be competition between the normal genomes and mutant RNA inside an infected cell. Many of the mutant RNAs would be unable to produce proteins which could assemble into a complete viral particle. Some of these RNA's would remain inside the cell, which would present opportunities for them to survive by evading the immune system. The normal viruses outside would be subject to attack by the immune system. So mutant genomes of polio virus could very well be selected for and be capable of surviving within a cell while normal viruses succumbed.

Another question I've thought about recently is why doesn't polio virus completely decimate all motor neurons? Why do some survive? Bodian's work in the 1940's showed that most all of the neurons appeared abnormal during the acute polio infection. Yet some survive, why? Does the infection with virus allow some neurons to modify themselves resulting in an effective defense mechanism against infection? Does the nerve cell surface change, or is there some other biochemical change which may persist after infection, which, ultimately shortens its life cycle and may result in PPS down the line?

Or do cells have within them now bits of polio virus RNA, which have survived all these years because of their evolutionary fitness in competition with all viral progeny? If so these RNAs surely make proteins within the cell and these proteins, no doubt, migrate to the cell's surface. There, they can be recognized by the immune system and attacked. Has this been going on very slowly? Naked RNA (without the virus capsid) can infect adjacent cells but this is very inefficient compared to intact polio virus. Has this been going on for 30 plus years? Are some or all of these proposed mechanisms in place and do they explain why post-polio motor neurons "wear out".

There is precedent justifying these questions. Coxsackievirus is a Picornavirus too. It is very similar to polio. One single gene mutation of coxsackievirus B3 can convert it into a virus, which damages the heart. *[1]*

The progression of HIV virus to AIDS is not clearly understood. The evolving virus, within cells, results in mutants at astonishingly high rates. This virus is highly adaptable and cannot as of yet be exterminated within a patient.*[1]* And highly mutated polio virus RNA was found in a study of a small number of patients with PPS. One half of patients with PPS (5) had recoverable highly mutated polio RNA. While none who had paralytic polio but no signs of PPS had recoverable mutated RNA. Was this due to damaged neurons that "wore out" releasing the RNA that the control group had? Or was the presence of this RNA causal to Post-Polio Syndrome?*[2]*

My advice mirrors Monod's at the start of this essay: don't embrace any of these ideas, be skeptical, question, and wait for evidence to arrive. Just think about it.

References

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