VIROLOGY

# Post-Polio Syndrome: Remembrance of Viruses Past

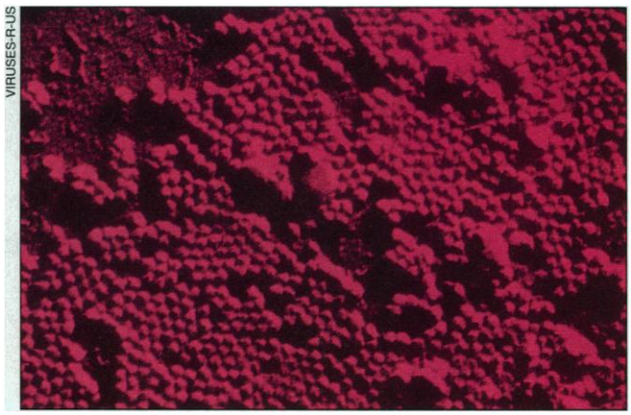
Images of polio—FDR in his wheelchair, rows of coffin-like "iron lungs"—have largely faded into history. Although the disease persists in parts of Asia and Africa, it was virtually eradicated from the United States in the 1950s by vaccines. But the specter of polio hasn't disappeared entirely from this country. Decades after suffering varying degrees of paralysis, nearly a third of the 1.6 million polio survivors have begun to develop puzzling ailments, such as fatigue, muscle weakness and atrophy, and in some cases difficulty breathing.

Lumped together under the term post-polio syndrome (PPS), these symptoms are now thought to afflict 500,000 people. But the cause of PPS remains a mystery—and the intrigue is growing. Two weeks ago, at a symposium sponsored by the New York Academy of Sciences,* three research groups announced finding fragmentary genetic sequences resembling polio virus in some PPS sufferers. That was startling, since most virologists assumed the virus had disappeared from the bodies of polio survivors long ago.

The discovery of the virus fragments suggests to researchers such as virologist Helena Kopecka of the Pasteur Institute that PPS could be the renewed assault of a lurking foe. But another camp is skeptical, particularly since only fragments—and no live virus—have been detected. The virus replicates quickly and bursts through the infected cell wall, so "it's difficult to conceptualize it harboring itself in a cell" for 40 years, says Marinos Dalakas, a neurologist at the National Institute of Neurological Disorders and Stroke (NINDS) and co-chair of the conference. Dalakas and other scientists suspect PPS results from the weakening of neurons that were damaged in the original attack.

Polio is caused by three strains of polioviruses and, on rare occasions, related viruses such as Coxsackie B. These viruses, all members of the enterovirus family, have RNA as genetic material and can infect the central nervous system and attack nerves that regulate muscle action. When former polio patients began reporting PPS symptoms in the 1980s, the thought of a renewed infection did occur to neurologists. Unable to culture a live virus from these patients, however, scientists discounted the notion.

But those skeptics got a surprise in 1991 when a team led by clinical neurochemist Mohammad Sharief of the National Hospital for Neurology and Neurosurgery in London found exactly the kind of immune response produced by an active polio infection in PPS patients. Sharief's team detected immunoglobin M (IGM) antibodies specific to poliovirus in 21 of 36 PPS patients, and none in the 67 controls (*New England Journal of Medicine*, 12 September 1991, p. 749).




**Unvanquished virus?** Some think resurgent polioviruses *(above)* are behind puzzling symptoms afflicting former polio victims.

Kopecka and her colleagues enlisted a molecular bloodhound to sniff out the actual virus—the polymerase chain reaction (PCR). At the Academy meeting, the Pasteur group reported that they had used PCR's ability to amplify minute genetic sequences to detect "polio-like sequences" of genomic viral RNA in the spinal fluid of five of eight PPS patients. The match wasn't identical—there were point mutations and other rearrangements—but Kopecka says the sequences were similar enough to poliovirus to "favor the persistence of poliovirus for several decades in PPS patients." And the virus should be active, since enteroviruses don't normally assume a latent form. Dalakas' lab has produced similar findings.

It's also possible that a new infection, not a resurgent attack, is behind PPS. Collaborating with Sharief, a team led by virologist Peter Muir of the United Medical and Dental Schools of St. Thomas' Hospital in London announced at the meeting that it had detected RNA that closely resembles that of Coxsackie B virus in three of 24 PPS patients. They could not find any such RNA in their control group, which included polio patients. One possibility, says Muir, is that "people who had polio in the past may be susceptible to infection from other enteroviruses." And new infections, in turn, might trigger PPS.

But the cases for new or long-smoldering viral infections have large holes. For one thing, scientists have been unable to culture any live enterovirus from a PPS patient. For another, other researchers haven't been able to detect the kind of strong antibody response that Sharief saw in PPS patients. Burk Jubelt, a neurologist at the State University of New York Health Science Center in Syracuse who failed to find a strong antibody response in his study, told the meeting his work "doesn't support the theory that poliovirus persistence is the cause of PPS."

The poliovirus-like fragments, Dalakas says, might be due to the virus mutating into a less aggressive form inside the neurons, which might then gradually slough off non-infective viral fragments over the years. In that case, Dalakas says, "the fragments may mean nothing" in relation to PPS. Other scientists are even more skeptical of the PCR findings. "PCR is notoriously fickle when it comes to detecting small amounts of RNA," says Joseph Melnick, a virologist and authority on enteroviruses at Baylor College of Medicine in Texas. Melnick argues that the fragments may very well be false positives.

If Dalakas and Melnick are right, another factor must explain the syndrome; Dalakas thinks it is nerve-cell attrition. According to this theory, the initial viral attack kills a number of motor neurons and weakens some of the surviving nerve cells. As the post-polio patient ages, these damaged neurons increasingly lose their connections to muscles, which stop responding. Several groups have seen this reduction in nerve-muscle connections in PPS patients.

Until a live poliovirus shows up in PPS patients, most neurologists favor attrition, says Johns Hopkins neurologist Richard Johnson, but he says he's keeping an open mind until further work is done. And one crucial experiment is underway: Researchers at NINDS and elsewhere are using PCR to search for poliovirus directly in spinal-cord neurons from dead PPS patients. If live poliovirus doesn't show up in these neurons, then Melnick and other researchers say the virus will have been banished from Western medicine—for the second time.

**–Richard Stone**

*"The Post-Polio Syndrome: Advances in the pathogenesis and treatment," Bethesda, Maryland, 27 to 30 April.