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Acute Polio and Post-Polio Syndrome

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Poliomyelitis, an infectious neurologic disease, holds an important place in the history of public health in the United States and internationally. Until the polio vaccines became available in 1955 and 1961, 20th century American families were faced with recurring polio epidemics. Children were most at risk. Today, polio is extremely rare in the United States, and efforts to eradicate the disease worldwide have paid off. However, the generation of survivors, who were impacted by polio as children in decades past are entering or have reached their older years. Many of these survivors are now experiencing a return of some symptoms, known as post-polio syndrome.

This opening chapter reflects on the historical and epidemiological contexts of polio and post-polio syndrome. It also describes the causes, pathology, and relationship between these two debilitating conditions.

A LOOK BACK

Most of us think of polio as an epidemic disease. Yet, it wasn't until the end of the 19th century when the first epidemic was recorded in Stockholm, Sweden. Before that, polio made many isolated appearances throughout history, beginning in the time of the ancient dynasties of Egypt. One example, and maybe the earliest case of recorded poliomyelitis, was discovered by archaeologists in an Egyptian mummy who died sometime around 3700 BC. Another example dating from 1400 BC shows a young Egyptian priest in a stone carving leaning on a staff with a shortened, deformed foot in the characteristic pose of a polio-affected limb.

The first comprehensive descriptions of polio in the medical literature were published in the 1800s by two European physicians, Dr.

Jacob von Heine and Dr. Karl Medin from Germany and Sweden, respectively. For a time, polio was known as Heine-Medin disease. In America, there were sporadic reports of poliomyelitis as early as 1841, but the first U.S. epidemic did not occur until 1894 near Rutland, Vermont. By 1913, polio had appeared in every state and province of the United States and Canada, afflicting more than 25,000 children and adults.

It was not until 1916, however, that polio even briefly took center stage in our national awareness. In that year, the first major U.S. epidemic occurred. More than 9,000 cases were reported in New York City alone, resulting in 2,400 deaths and panic in the streets. The vast majority of those affected were under the age of five years, which led to the name “infantile paralysis.” Although scientists had identified the poliovirus in 1908, there was wild speculation by the lay public about the cause of this frightening disease, including everything from “stray cats to doctors’ beards to radio waves.”

Five years after the epidemic of 1916, Franklin Delano Roosevelt contracted “infantile paralysis” at the age of 39 years, and the course of polio history was changed forever. Although his legs were badly paralyzed, FDR never lost faith that he might walk again. With remarkable courage and a flair for denial, Roosevelt continued his political career and private life masking his disability.

Over the years and during his frequent visits to Warm Springs (the great polio Mecca he established in southern Georgia), FDR stayed in touch with other polio survivors and actively supported the search for better treatments and a vaccine. This commitment ultimately led to the creation in 1937 of the National Foundation for Infantile Paralysis (later known as the March of Dimes). During the next two decades, the March of Dimes played a central role in raising the funds needed to develop the polio vaccines.

A Seemingly Unstoppable Disease

During the 1930s, 1940s, and 1950s, the U.S. polio epidemics seemed unstoppable. As they grew in size, they became more deadly, creating a climate of fear and awe that is difficult to imagine today. From 1951 to 1955, approximately 40,000 cases were reported each year, with infections increasingly striking at older children and young adults. Starting in 1951, an effort was made to improve the accuracy of diagnosis and to report cases as either paralytic or nonparalytic. Perhaps partly because

of this effort, the next year, 1952, became the largest epidemic year on record when 52,000 cases were reported. Of these, more than one-third had paralysis and more than 3,000 persons died.

By 1953, more American children died of paralytic poliomyelitis than any other communicable disease. Unlike the current HIV/AIDS epidemic, polio haunted everyone. Families stayed at home, swimming pools were closed, and public events were canceled. Children, in particular, were at risk, especially during the hot summer months. As one observer commented, polio seemed to seek out children, the most vulnerable among us.

At all ages, polio affected males slightly more than females. Paralytic polio was more common in the middle and upper classes than in the lower classes. The explanation for this socioeconomic difference was that children in lower classes, who tend to live in more crowded situations with poorer sanitation, were more likely to be exposed to the virus at a young age when the illness was generally milder and lifetime immunity (natural protection) was acquired.

All races contracted the disease in proportion to their representation in each socioeconomic class, although in the later epidemics the death rate was higher among African Americans, who often had less access to specialized treatments, such as the iron lung. In early epidemics, when no treatment existed, death rates among the races were similar.

Questions About Epidemics Remain

Epidemic poliomyelitis was found throughout the United States in rural and urban settings alike, with particularly high rates in the growing suburbs of post-World War II America. Epidemics peaked and ebbed from year to year and were usually explained in two ways: first, by environmental conditions that either encouraged or discouraged transmission of the disease and second, by variations in the strength of different strains of the poliovirus passing through a population. Even though an enormous amount of scientific information is known about polio, it remains a curious fact that there is still no fully satisfactory explanation of why and where epidemics occurred in any given year.

It's also likely that the actual number of people infected by polio was much higher than the number of cases reported. As will be discussed later in this chapter, the vast majority of individuals who are infected with the poliovirus have mild, flu-like symptoms that resolve within a few days. Only a small number (less than 5 percent) actually develop

symptoms of muscle weakness or paralysis that would prompt them to seek medical treatment and be diagnosed with a polio infection.

THE POLIO VACCINES

On April 12, 1955—10 years to the day after FDR's death—it was announced in a dramatic national radio and television broadcast that the Salk vaccine was both safe and effective. It was a triumphant moment for U.S. medicine and brought enormous pride and relief to the American people. To use a metaphor of the time, the war against polio was over. Newspapers carried full-page headlines such as “Polio Conquered” and “Victory Over Polio.” American technology had won. Towns across the country held parades with marching bands and signs reading “No More Polio,” “Thank you, Dr. Salk,” and “Our children are safe again.”

Salk immunization, given by injection, uses killed or inactivated virus particles. The vaccine is usually called IPV, for inactivated polio vaccine. Because the virus is killed, the vaccine is extremely safe and cannot cause new cases of polio. Six years after Jonas Salk's extraordinary triumph, Albert Sabin's vaccine became available in 1961 following testing in Russia. The Sabin vaccine uses live, but attenuated or “weakened” virus particles, and is given by mouth. For this reason, it is often called OPV, or oral polio vaccine. Because the weakened OPV virus can be “passed” from person to person, thus immunizing many other individuals with a single dose, the Sabin vaccine is considered superior to the Salk vaccine. However, the Sabin vaccine has the great disadvantage of producing paralytic polio in an extremely small number of recipients (approximately 1 out of 700,000 individuals after the first immunization).

Following the widespread use of the vaccines, the incidence of polio dropped dramatically in the mid and late 1950s. During the next two decades, polio almost disappeared. In 1979, 24 years after the introduction of the Salk vaccine, the last case of paralytic polio caused by a live naturally occurring virus was reported in the United States.

Tragically, despite this extraordinary accomplishment, acute polio was still being reported until the mid-1990s. Approximately 10 to 12 new cases of paralytic polio were caused each year by the weakened virus in the Sabin vaccine, which was the vaccine recommended by the federal government. Most of the affected individuals became paralyzed because of an immune deficiency (an abnormality of the body's defense

mechanism). Such deficiencies reduce the body's ability to fight infections, making it easier, even for weakened viruses, to gain a foothold and cause serious illness.

Because vaccine-related polio is completely preventable with the use of the Salk vaccine, the U.S. government changed its policy in 2000. It now recommends that four immunizations with IPV be given during infancy and OPV be used only in very special circumstances.

Worldwide Progress

Meanwhile, at the global level, the efforts of the World Health Organization, Rotary International, and other organizations to eradicate polio are beginning to pay off. In 1996, the number of officially reported polio cases was under 4,000. Using "national immunization days," which are the main tool of the polio eradication campaign, many countries have been able to completely eliminate polio. On a single day, in January 1997, approximately 127 million children in India were vaccinated against polio in what is believed to be the largest health event ever organized by a country. If polio is eradicated from the world, it will join smallpox as only the second disease humankind has successfully eliminated from the globe.

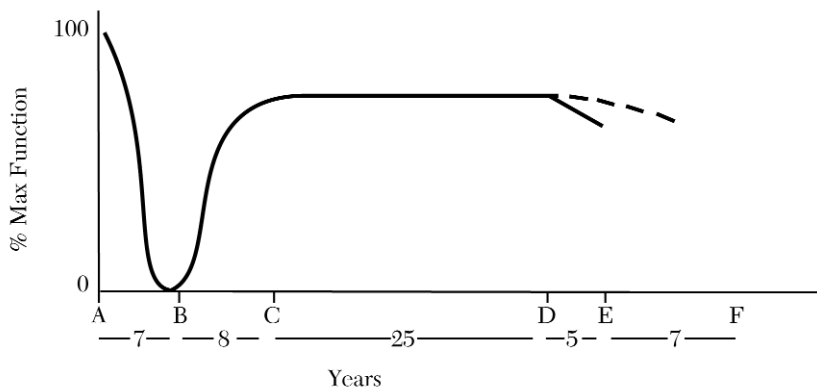
THE FOUR STAGES OF POLIO

Historically, polio has been divided into three fairly distinct stages: acute illness, the period of recovery, and stable disability. In the early 1980s, clinicians and researchers began to realize that there was a fourth stage characterized by the onset of new symptoms related to the original polio attack. This stage has been described by various terms, including "the late effects of polio," "post-polio sequelae," "post-polio progressive muscular atrophy," "post-polio muscle dysfunction," and "post-polio syndrome." The names "post-polio muscle dysfunction" and "post-polio progressive muscular atrophy" emphasize abnormal muscle function. This narrow focus makes these terms more appropriate for research. By contrast, "post-polio syndrome," or PPS, is more broadly defined, making it more practical for clinical purposes. In addition, the term post-polio syndrome has been widely used in the medical and consumer literature for many years. For these reasons, PPS is used in this book.

Figure 1.1 shows the typical course for the three traditional stages of

paralytic polio as well as the beginning of Stage IV or PPS. These health and functional changes are based on the acute and chronic polio experience of a group of persons evaluated at the post-polio clinic in Houston, Texas.

Figure 1.1 Natural History of Polio



Legend: Health and functional changes showing the four stages of polio for 132 individuals with PPS evaluated at the post-polio clinic in Houston, Texas. A = birth; B = onset of acute polio or Stage I (average age of seven years); B to C = period of recovery or Stage II (an average of eight years); C to D = maximum recovery and period of neurologic and functional stability or Stage III (an average of 25 years); D = onset of PPS or Stage IV (B to D an average of 33 years); E = time of clinic evaluation (D to E an average of five years); F = death (E to F: unknown). Dashed line = projected course without PPS.

Stage I: Acute Illness

The onset of polio is characterized by a mild fever, headache, sore throat, diarrhea or vomiting, and malaise (a general sense of not feeling well). Initial symptoms are similar to those of many other viral illnesses. In the great majority of individuals, these symptoms are gone within two or three days. It is unlikely that these individuals are even diagnosed with a polio infection. In less than 5 percent of those who contract the poliovirus, the symptoms are more severe, reflecting a viral invasion of the central nervous system (CNS), which consists of the spinal cord and brain. Infection of the CNS results in a sharp escalation of symptoms with high fever, stiff neck, severe headache, and muscle pains. In some people, the disease stops there and no weakness or paralysis ever occurs. In others, approximately 1 percent to 2 percent of those affected, the infection continues to spread, producing variable amounts of muscle paralysis or weakness in the limbs, trunk, and even the face and neck.

During the widespread epidemics of the 1940s and 1950s, roughly 12 percent of those who developed acute paralytic poliomyelitis died from breathing or swallowing complications.

Stage II: Period of Recovery or Convalescence

Recovery begins as soon as an individual's temperature returns to normal and the other symptoms subside. This stage can last from weeks to years, depending on the severity of involvement and age at onset. Persons who contract polio as children or infants and have extensive paralysis take the longest time to recover. During this period, individuals usually begin an intensive program of rehabilitation in hospital or home with the goal of strengthening and retraining weakened muscles and learning to regain lost function. For the group of persons described in Figure 1.1, the average length of Stage II was eight years.

Stage III: Stable Disability or the Stage of Chronicity

Stage III begins when a person reaches a plateau of maximum recovery of strength and stamina. The precise time when this stage starts may be hard to determine, especially if the individual is still growing and changing developmentally or is undergoing reconstructive surgery to enhance strength and function. Despite these difficulties, most people have a general idea of when their recovery was complete.

Stage IV: Post-Polio Syndrome

The third stage of polio lasts indefinitely for many individuals, perhaps for the majority who had paralytic polio. For some polio survivors, the stage of stable disability ends and Stage IV—or PPS—begins with the onset of new weakness. This weakness is often accompanied by other symptoms, such as fatigue, pain in muscles or joints, and decreased function. For the individuals described in Figure 1.1, Stage III lasted an average of 25 years. Stage IV began, on average, 33 years after the acute onset of polio. A similar interval is found in other studies, but the range has been reported to extend from two decades to eight decades.

DEFINITION OF POST-POLIO SYNDROME

Post-polio syndrome is a neurologic disorder that produces a cluster of symptoms in individuals who had paralytic polio many years earlier.

Because these symptoms tend to occur together, they are called a syndrome. Typically, these problems occur after a period of functional and neurologic stability of at least 15 years following the initial episode of polio and include new weakness, fatigue, decreased endurance, and loss of function. Some researchers also include pain, especially in muscles and joints, as part of the syndrome. Less commonly, the symptoms include muscle atrophy (shrinkage), breathing and swallowing difficulties, and cold intolerance.

Some of the symptoms (such as weakness, fatigue, and atrophy) appear to be caused by a progressive degeneration or impairment of motor units (Figure 1.2). Other symptoms (such as muscle and joint pain) are more likely the result of excessive wear and tear on different parts of the musculoskeletal system, although this wear and tear can be brought on or made worse when muscles become weaker.

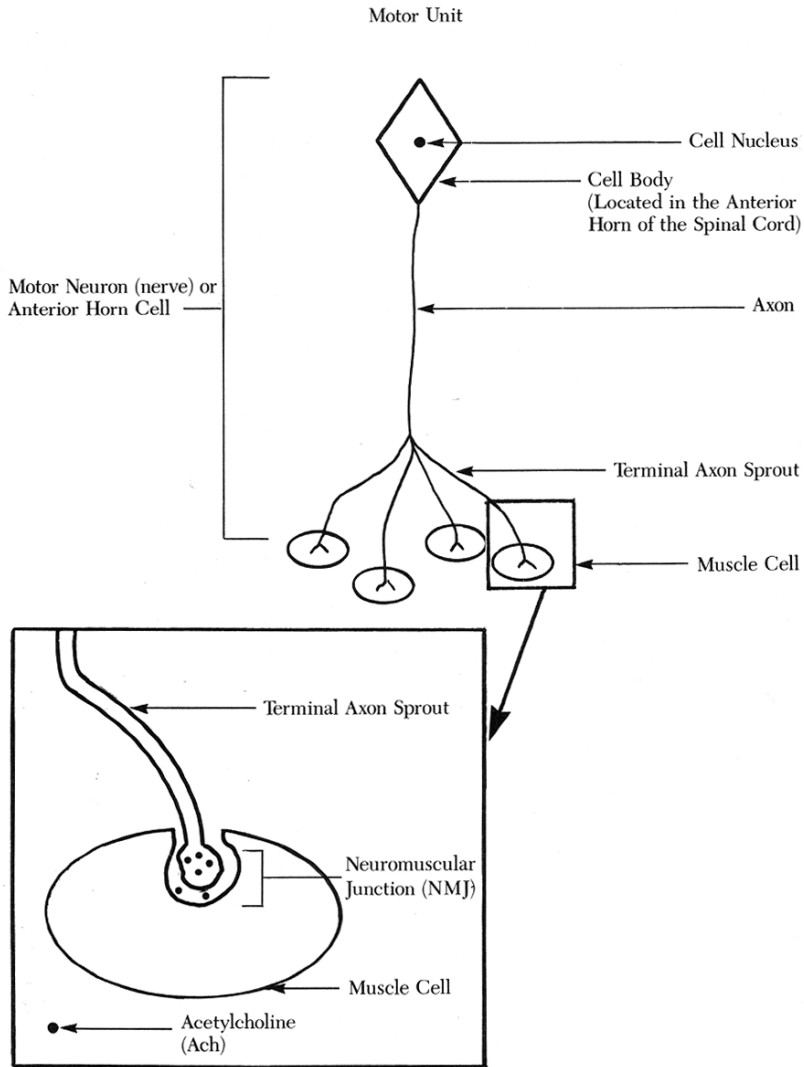
The percentages of new health and functional problems reported by persons evaluated in several post-polio clinics are presented in Table 1.1. The most common problems are fatigue, weakness, and pain in muscles and joints. The new weakness is located in muscles previously affected by polio, as well as in muscles thought to be unaffected by the original illness. At first glance, the phenomenon of “unaffected” muscles becoming weak seems contradictory but, in fact, it is well-documented. Usually, it means that the polio was so mild in those muscles at the time of the original illness that the individual, as well as health

Table 1.1 New Health and Functional Problems

Symptom	Percent (Range)
HEALTH PROBLEMS	
Fatigue	86–87
Muscle pain	71–86
Joint pain	71–79
Weakness	
Previously affected muscles	69–87
Previously unaffected muscles	50–77
Cold intolerance	29–56
Atrophy	28–39
ADL PROBLEMS¹	
Walking	64–85
Stair climbing	61–83
Dressing	16–62

¹ADL = Activities of daily living

Figure 1.2 The Motor Unit



Legend: The motor unit consists of a motor nerve or anterior horn cell (cell body, axon, and axon sprouts) and all the muscle cells stimulated by that nerve. The cell body (which regulates the motor nerve functions) is located in the anterior horn of the spinal cord. Axons are just short or long enough to reach the muscles they stimulate to contract. Axons that supply muscles in the legs can be three or more feet in length. The insert shows a close-up view of the neuromuscular junction. This is where the terminal axon sprout stimulates the muscle cell to contract by releasing the chemical acetylcholine (Ach).

care professionals, were unaware of any polio involvement in those particular limbs. Yet, there was enough loss of motor neurons that new weakness developed after many years of overuse. The most common new functional problems include increased difficulty in walking, climbing stairs, and dressing—activities that require repetitive muscular contractions.

THE HISTORY OF POST-POLIO SYNDROME

For more than 100 years, the late effects of polio have been known to occur in some individuals many years after their initial illness. The first descriptions appeared in 1875 in the French medical literature. The cases involved three young men who had paralytic polio in infancy and developed significant new weakness and atrophy as young adults. These new problems occurred in muscles previously affected by polio and in muscles thought to be spared. All of the subjects had physically demanding jobs that required strength and repetitive activities.

In a commentary on one of the cases, the great 19th-century French neuropathologist, Jean Martin Charcot, suggested several hypotheses for these changes. He believed an initial disease of the spinal cord (such as polio) might leave some individuals more susceptible to a subsequent spinal disorder. He also hypothesized that the new weakness was caused by overuse of the involved muscles. His observations are surprisingly relevant to the current understanding of PPS.

After those initial reports, there was only sporadic interest in the late effects of polio for many decades. In the century following Charcot's observations, fewer than 35 reports were published, describing less than 250 cases. As with the first subjects, these reports described new problems that included weakness, atrophy, and fasciculations (involuntary muscle contractions or twitching), occurring up to 71 years after an attack of paralytic polio.

Why these aftereffects of polio remained an obscure and largely unexplored area of medicine until recently is not clear. Few diseases are as widely prevalent in the world or have been as intensively investigated as polio. Because of the rapid and dramatic onset of symptoms, polio was viewed as a classic example of an acute viral infectious disease. As a result, most of the scientific energy and resources were directed at early management and prevention with virtually no research into long-term sequelae, or aftereffects. Until recently, medical textbooks classified paralytic polio as a static or stable neurological disease.

New Problems Appear

With widespread use of the vaccines, polio quickly became a medical oddity in the industrialized world, and interest and funding in polio-related problems waned. However, polio and its complications only appeared to have been defeated. Because the major epidemics occurred in the 1940s and 1950s, and new neurologic changes appeared 30 years to 40 years later, many thousands of polio survivors did not begin to experience new problems related to their polio until the late 1970s and early 1980s.

By sheer weight of numbers, persons experiencing PPS finally started attracting widespread attention in the early 1980s. The term “post-polio syndrome” was coined at about the time of the first International Post-Polio Conference at Warm Springs, Georgia, in May 1984. In the intervening years, there has been a marked increase in the attention focused on PPS by researchers and clinicians, leading to a more precise definition, a better understanding of possible causes, and development of more effective management.

EPIDEMIOLOGICAL ASPECTS OF POST-POLIO SYNDROME

Accurate totals of the number of Americans who had poliomyelitis are not available and probably never will be. There is no national registry of persons who had polio, and there is no way, after all these years, to compile accurate figures from state and local health departments. Finally, because 95 percent of people who contracted polio had a mild illness that most likely went undiagnosed and untreated, many polio survivors are likely unaware of their history of infection. The best estimate of the number of polio survivors in the United States is based on data from the government’s National Center for Health Statistics, which conducts the National Health Interview Survey (NHIS) each year. This survey collects data from a representative sample of the U.S. population regarding their health, including any disabilities they may report. These results are then used to estimate the number of people in the country with various health conditions.

In 1994 and 1995, NHIS surveyors specifically asked respondents if they had ever been diagnosed with poliomyelitis (National Center for Health Statistics, 2000). If they reported that they had been diagnosed with polio, the survey participants were asked several additional ques-

tions about their original polio infection, its treatment, and their current health status. At the time of the survey, an estimated 920,000 U.S. residents identified themselves as polio survivors. Of these persons, 391,500 were affected by paralytic polio. All polio survivors were asked if they had been diagnosed with PPS by a physician, and 11 percent of survivors indicated that they had. They were also asked if they believed they were suffering from PPS; 25 percent of polio survivors answered affirmatively.

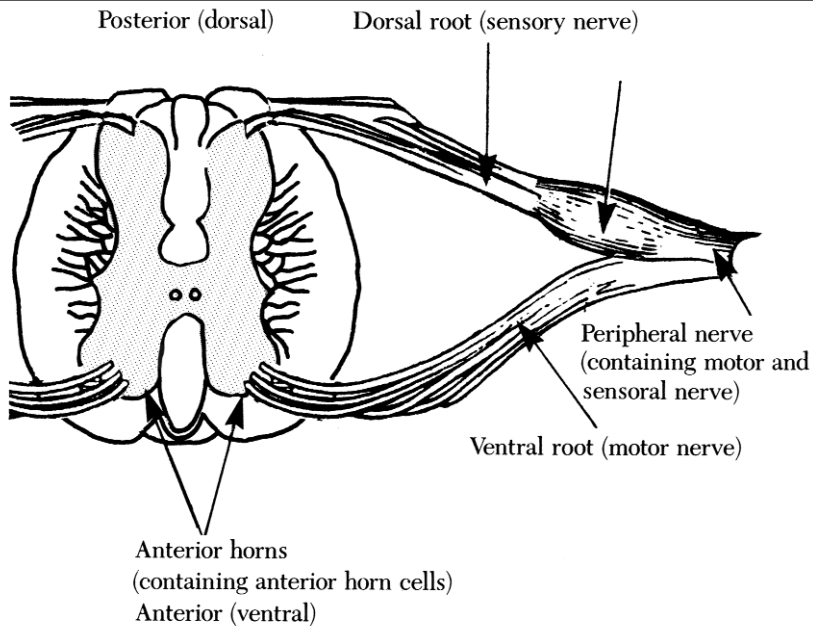
This difference in the number of those who reported a diagnosis of PPS and those who believe that they have it may be the result of several factors. It may be that a number of them have PPS but have not yet received a correct diagnosis. It may also be the case that they have symptoms of PPS that are actually being caused by another condition. (Other researchers have reported that up to 70 percent of polio survivors may be experiencing symptoms of PPS. Many of those estimates are based on studies involving polio survivors who seek clinical care for their symptoms, and so don't take into account the many survivors who have not had further problems related to their polio. This may result in over-estimations of the actual number of polio survivors affected by PPS. In contrast, the NHIS collected data from all self-identified polio survivors, regardless of whether or not they were experiencing new problems related to polio; this most likely is the reason for the lower estimate of how prevalent PPS actually is among survivors.)

The issue with these figures, however, is that they reflect the number of survivors based on a survey conducted 10 years ago, and so they do not reflect the number of survivors who are still alive today. Given that half of those surveyed in 1994 and 1995 were younger than 55 and over 80 percent were under the age of 70, it is reasonable to estimate that there are more than 700,000 survivors currently living in the United States. Several studies indicate that a large number of survivors, perhaps 60 percent or more, are experiencing one or more new difficulties related to old polio, such as muscle aches and joint pains. However, the number with PPS (new weakness with or without other symptoms many years after acute polio) is undoubtedly smaller, more likely in the range of 11 percent to 25 percent or between 81,000 and 184,000 survivors of the 700,000.

THE RELATION OF ACUTE POLIO TO POST-POLIO SYNDROME

The word poliomyelitis comes from the Greek, *polios*, gray, and *myelos*, marrow, and the English ending, *itis*, inflammation. When seen in cross-section, the spinal cord has both white and gray areas. The poliovirus produces an inflammation of the gray marrow portion of the spinal cord located in the front, or anterior, part of the cord (Figure 1.3). This area is called the anterior horn; the nerve cells clustered there are called anterior horn cells. Because poliovirus attacks almost exclusively the motor nerve cells in the anterior horn of the spinal cord, physicians sometimes refer to polio as an anterior horn cell disease or AHCD. The acute infection is caused by one of three types or strains of poliovirus called Types I, II, and III. Type I is often responsible for the most severe paralysis. These types are sometimes confusing as the same word is used to describe the clinical types of polio, e.g., spinal, bulbar,

Figure 1.3 Cross-Section of the Spinal Cord



Legend: The cross-section of the spinal cord showing both white and gray areas. The anterior horn appears gray due to the clustering of anterior horn cells. The white matter consists of nerves covered with a whitish insulation material called myelin. The peripheral nerve shown here is a "mixed" nerve and is formed by a posterior (sensory) nerve and an anterior (motor) nerve. Some peripheral nerves have only a sensory component and others only a motor component.

or spinal-bulbar. However, the virus type is not related in any way to the clinical type of illness. After an individual has been infected with one strain of virus, the body develops lifelong immunity protecting it from reinfection with that type of virus ever again. The three types of viruses are immunologically distinct (because of differences in their protein coats), so infection with one does not provide protection from the others. This phenomenon explains why some individuals have had polio twice and why, in theory, it is even possible to have it three times.

What Happens After Acute Infection

Acute infection occurs when the virus enters the body through the mouth from water or food contaminated with feces. Following multiplication in the tissues of the throat and intestine, the virus passes harmlessly from the gut or it penetrates the intestinal wall and travels in the blood to all parts of the body. The great majority of infected individuals have no symptoms or experience a self-limited illness characterized by fever and gastrointestinal upset for several days. In 1 percent to 2 percent of the infected population, the virus invades the spinal cord by traveling up the motor neurons to the anterior horns, where it can result in a variable amount of paralysis.

Regardless of the extent of paralysis, however, the virus is widely distributed, typically infecting more than 95 percent of the motor neurons in the spinal cord and many other cells in the brain as well. Following this invasion, cells die or shed the virus and regain a normal or near-normal appearance. Whether these recovered motor neurons are more likely to sustain injury or begin to malfunction later in life is unknown. If they are more easily injured or overworked, it might provide one explanation for the new weakness in those with PPS.

To gain a better understanding of what happens to nerves and muscles after a bout of acute polio, it is useful to review some basic anatomy. Figure 1.2 shows a motor nerve cell or motor neuron (comprising a cell body, a long tentacle called an axon, and axon sprouts). The sprouts, or rootlets, which branch out at the end of the axons, are called terminal axon sprouts. Each terminal axon sprout stimulates an individual muscle cell to contract. Together, the motor neuron and the muscle cells supplied by that neuron are called the motor unit.

Following an acute attack of polio, some motor neurons die and others survive. The ones that survive can develop additional terminal axon

sprouts. Their function is to reconnect (reinnervate) nerves to muscle fibers left “orphaned” by the death of their original motor neurons (Figure 1.4, B and C).

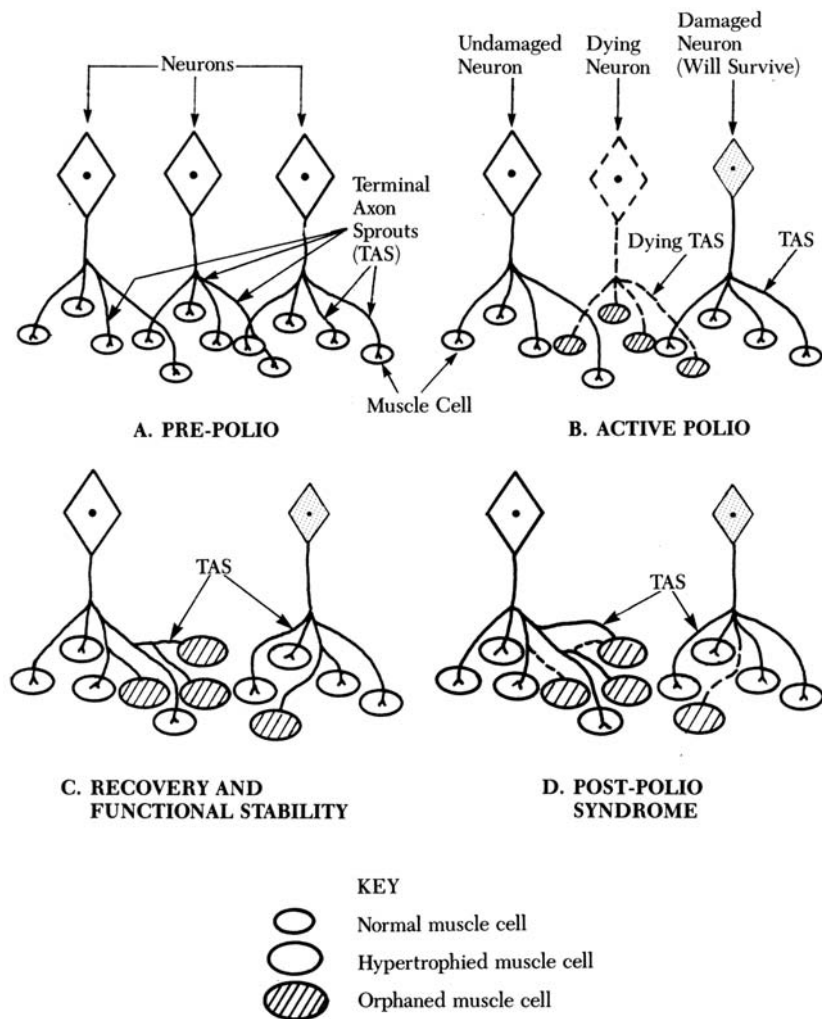
Keeping Muscle Cells Working

In a sense, the growth of axon sprouts is the body’s effort at a rescue mission to keep as many muscle cells alive and working as possible. This compensatory process allows an uninfected or recovered motor neuron to adopt as many as seven, eight, or even 10 additional muscle fibers for every muscle cell stimulated by that nerve originally. This process means a single motor neuron that was designed to supply 1,000 muscle fibers might eventually be redesigned to stimulate as many as 10,000 fibers or a total of 9,000 extra muscle cells beyond its original capacity. Thus, the size of many motor units increases significantly after acute polio, resulting in what are called giant motor units. These giant motor units make it possible for a few motor neurons to do the work of many (Figure 1.4, C).

In addition to the extra sprouting that makes giant motor units, the other major mechanism that produces a return of strength is muscle cell hypertrophy (enlargement), which develops in response to exercise. Combined, these mechanisms of compensation (axon sprouting and hypertrophy) explain how persons experienced what appeared to be a miracle cure, going from bed to wheelchair to walking over a period of six months to 12 months.

During the ensuing interval of stable strength and endurance (Figure 1.1, Stage III), it appears to the individual that recovery has been completed. Yet, as it turns out, the compensatory mechanisms keep right on working. If old terminal axon sprouts drop off (producing a disconnection between nerves and muscles or denervation), new sprouts take their place (producing a reconnection or reinnervation). This process of denervation balanced with reinnervation, combined with new hypertrophy, results in a steady state or dynamic equilibrium that helps maintain a constant level of strength. When this steady state is disrupted after many years, a critical threshold is crossed and new weakness occurs, marking the onset of PPS.

The NHIS data support this relationship between the original polio infection and the later development of PPS (National Center for Health Statistics, 2000). In that survey, people who reported having a more widespread polio infection (characterized by having a large number of

Figure 1.4 Motor Neurons and Muscle Cells Before and After Polio

Legend: A = pre-polio; three normal motor neurons and the muscle cells they supply; B = acute stage of polio. The motor neuron on the left is not invaded by the poliovirus and remains undamaged. The middle neuron is infected and dies and the entire nerve disintegrates. The muscle cells (shaded) become "orphaned" or "stranded." The motor neuron on the right is infected with the virus but survives; C = the stages of recovery and functional stability. The orphaned muscle cells are "adopted" or re-connected to the surviving motor neurons by the growth of new terminal axon sprouts (TAS) creating "giant motor units." When these muscle cells become re-connected and start working again, the individual regains lost strength. Note the enlarged or hypertrophied muscle cells which develop in response to exercise. These enlarged cells also help increase an individual's strength; and D = PPS. In the two remaining motor neurons, some terminal axon sprouts are dying and new ones have grown. However, not all orphaned muscle cells become reconnected to motor neurons, leading to new weakness.

limbs or muscles affected, as well as by needing to be hospitalized for treatment of their polio) were more likely to report having been diagnosed with PPS. In addition, those who contracted polio as adults were more likely than those who had contracted polio as children to be diagnosed with PPS. This finding may reflect the observation that adults who contracted polio had more severe cases. No difference between men and women in the likelihood of diagnosis was found.

Table 1.2 Factors Associated with the Report of a Diagnosis of PPS

Characteristics of polio survivors who were more likely to report a diagnosis of PPS	Characteristics of polio survivors that were not found to be associated with a diagnosis of PPS
<ul style="list-style-type: none"> • Contracted polio as an adult • Reported having five or more muscle groups affected by polio • Reported having been hospitalized for treatment for polio 	<ul style="list-style-type: none"> • Contracted polio as a child or teen • Reported having three or fewer muscle groups affected by polio • Reported not having been hospitalized for polio • Gender • Personality characteristics related to motivation and personal drive

Source: National Center for Health Statistics, 2000.

THE CAUSE(S) OF POST-POLIO SYNDROME

No universal agreement exists about the cause of PPS. A growing consensus is developing among researchers, however, that the major symptom of PPS, new progressive weakness, is caused by a degeneration of the motor units. This explanation is not surprising because we know already that the motor unit is the primary target of the poliovirus during the original illness. To take this understanding one step further, data from a large number of studies by many researchers suggest that motor unit degeneration may occur at three separate levels, reflecting three different defects, or abnormalities.

One possible abnormality is at the level of the motor neuron, where there is a deterioration of the terminal axon and old sprouts that drop off are not replaced by new ones. A second abnormality involves a defect at the level of the neuromuscular junction (NMJ). The NMJ is the site where each motor neuron stimulates individual muscle cells to contract by releasing a chemical called acetylcholine or Ach (Figure

1.2). The current hypothesis is that too little Ach is made or released, resulting in a defect that causes diminished contraction of the muscle or no contraction at all. (This defect can be temporarily improved in some individuals using pyridostigmine, or Mestinon[®], which works by enhancing the effect of Ach at the neuromuscular junction.) A third abnormality may occur at the level of the muscle cell itself, resulting in decreased strength when the muscle contracts. How much muscle cell changes contribute to the overall picture of new weakness is uncertain.

Other Theories

Does this complete our understanding about the cause of PPS? Unfortunately not, as the underlying reason why motor units start to fail in the first place is still a mystery. Among many theories, probably the most likely is that of overuse. This theory is based on the assumption that the greatly enlarged motor units that drive post-polio muscles have labored for decades under an increased burden just to maintain everyday activities. This increased burden, or overuse, eventually might result in a degeneration of the motor unit after a certain number of years.

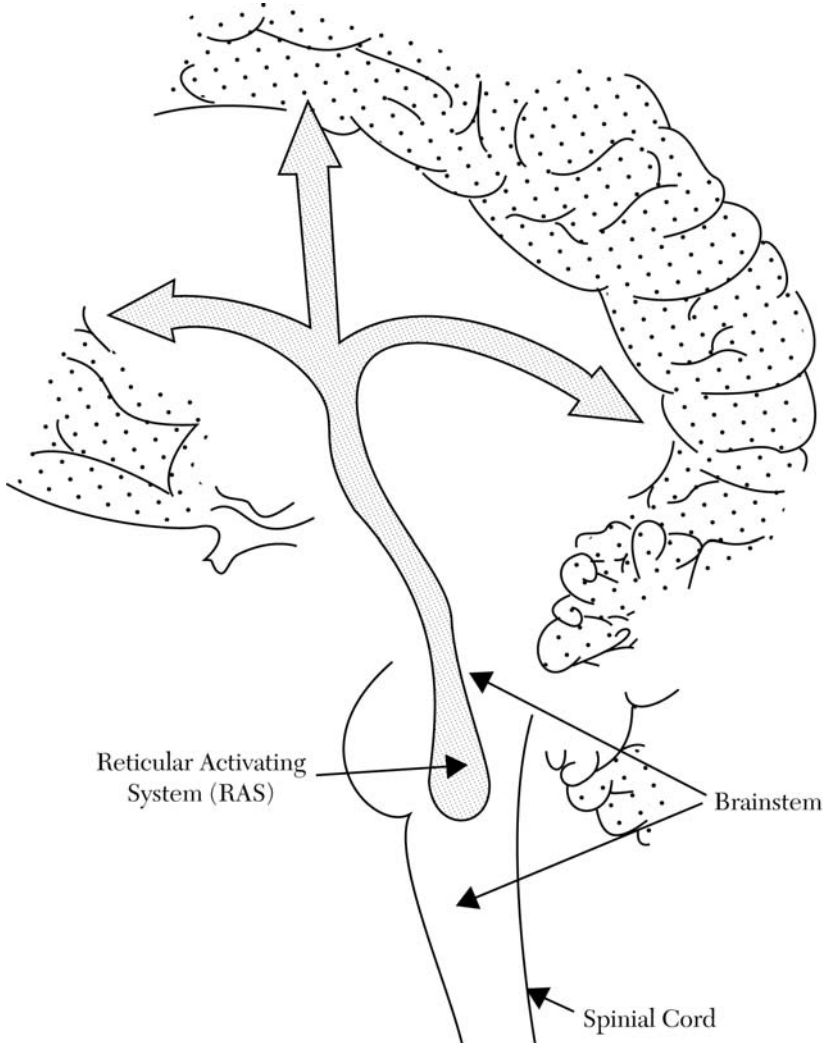
In addition to overuse, numerous other hypotheses have been proposed to explain the progressive weakness of PPS. These hypotheses include premature aging of the motor units, persistence of poliovirus fragments, an inflammatory or autoimmune process, environmental toxins that injure motor neurons, changes in the spinal cord (such as scarring), muscle overuse, and hormone deficiencies. In recent years, researchers in Sweden have reported evidence supporting the inflammatory hypothesis with preliminary findings that suggest some of the symptoms of PPS can be improved with intravenous immunoglobulins.

New Weakness Versus Fatigue

Of all the symptoms of PPS, new weakness is the easiest to study and, thus, has stimulated the most research. The results from this body of research have provided a better understanding of this symptom than any other aspect of PPS. Ironically, the symptom of fatigue is more common than new weakness in most studies but, because it is more difficult to investigate, much less is known about the cause. In addition, fatigue is an imprecise term with several meanings. In the context of PPS, people are sometimes referring to muscle fatigability or the muscle fatigue

that occurs with repetitive muscle contractions. This condition is easily demonstrated in a weak muscle when it is given a small amount of resistance and does not produce as much force on the fifth, seventh, or tenth contraction as it does on the first. This phenomenon is called peripheral fatigue and is probably caused by motor unit degeneration

Figure 1.5 Side View of Brain and Brainstem



Legend: A cutaway side view of the brain and brainstem. The dark arrows represent specialized tracks of the ascending reticular activating system (RAS) which helps maintain wakefulness and mental alertness.

and the same mechanisms that produce new weakness.

In addition to peripheral fatigue, another type is known as central, generalized, or brain fatigue. For many individuals, this type is the most disabling symptom of PPS. It is characterized by the rapid onset of mild to extreme tiredness, generalized headache, difficulty in concentrating, and general malaise. The origin of central fatigue is unknown, but one possibility is that it may also be caused by motor unit abnormalities—either at the level of the degenerating terminal axons or perhaps in the muscle itself, or both.

Another explanation for central fatigue locates the problem in the brain rather than in the motor unit. This theory suggests that central fatigue may be caused by abnormal function of a group of cells in the brain called the reticular activating system (RAS) (Figure 1.5). These cells were often invaded and possibly damaged by the polio virus during the acute illness. The cells in the RAS are responsible for maintaining wakefulness and mental alertness. Unlike the anterior horn cells in the spinal cord, which can be studied rather easily, there are no simple techniques to investigate the cells of the RAS directly. Much less is known, therefore, about their possible abnormal function.

IMPORTANT POINTS TO REMEMBER

- Poliomyelitis first appeared in the medical literature in the 1800s, but the first widespread polio epidemic in the United States occurred in 1916.
- Polio vaccines came into use in 1955 and 1961 and the incidence of the disease dropped dramatically.
- Polio occurs in four distinct stages: acute illness, the period of recovery, stable disability, and post-polio syndrome (PPS). Typically, the fourth stage, PPS, is associated with new weakness, generalized fatigue, and pain in muscles and joints.
- The new weakness occurs only in those muscles and nerves originally infected by the poliovirus and is believed to be caused by a degeneration or breakdown of affected motor units. The cause of generalized fatigue is less well-understood.

References are listed in Appendix C.

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