CHAPTER 34

Poliomyelitis and the Post-Polio Syndrome

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In the first half of the this century, epidemics of poliomyelitis (polio) ravaged the world. In the epidemic of 1952, over 20,000 Americans developed paralytic polio. With the introduction of the Salk inactivated polio vaccine (IPV) in 1954 and the Sabin oral polio vaccine (OPV) in 1961, the number of paralytic cases decreased to a handful per year. Polio had vanished and no longer was on the consciousness of Americans. The elimination of polio was a tremendous achievement for science and American medicine. However, in the late 1970s, survivors of paralytic polio began to notice new health problems that included fatigue, pain, and new weakness, thought not to be “real” by the medical establishment. The term “post-polio syndrome” (PPS) was coined by these patients to emphasize their new health problems.

This chapter reviews acute poliomyelitis and the related PPS.

POLIOMYELITIS

History

Poliomyelitis has occurred sporadically from 1600 to 1300 BC (1); however, epidemic poliomyelitis is a modern disease related to improved sanitation and human hygiene of the Western world (2). The first epidemics occurred in Europe in the mid-1800s and in North America in the 1890s. In 1870, Charcot and Joffroy ascribed flaccid paralysis to anterior horn cell damage. In 1905, Wickman recognized that asymptomatic infection and transmission occurred via the gastrointestinal tract (3). In 1909, Landsteiner and Popper (4) transmitted poliomyelitis to monkeys by the intracerebral inoculation of human brain tissue homogenates. In 1949, Enders et al. (5) cultured poliovirus in nonneural tissues, eliminating animals for pathogenetic studies, and the three poliovirus serotypes were also recognized (6,7).

The most important development in the history of poliomyelitis was the introduction of polio vaccines. They decreased the incidence of paralytic poliomyelitis in the United States to fewer than 10 cases per year (8,9). Recent developments have included the cloning and sequencing of several strains of the three types of poliovirus (10-17) and the resolution of the viral structure to 29 nm by x-ray crystallography (18). These techniques have made it possible to determine the precise viral coat amino acids that induce antibody responses (19) and the location and the amino acid sequence of the site on the virus for cellular attachment (16,18,20). The poliovirus receptor on the cell membrane has been identified and is a member of the immunoglobulin superfamily (21).

Clinical Manifestations

Definitions and Nomenclature

Poliavirus infections can be divided into minor and major forms (22) (Fig. 1). The minor illnesses occur 1 to 3 days before the onset of paralysis, with gastrointestinal complaints of nausea and vomiting, abdominal cramps and pain, and diarrhea and the systemic manifestations of sore throat, fever, malaise, and headache.

The major illness includes all forms of central nervous system (CNS) disease caused by poliovirus, including aseptic meningitis or nonparalytic polio, polioencephalitis, bulbar polio, and paralytic poliomyelitis, alone or in combination. It can follow the minor illness immediately or more often within 3 to 4 days or occur without the minor illness. It is common for patients to have aseptic meningitis recognized by stiff neck, back pain, photophobia, and headache before the onset of paralytic polio. Polioencephalitis precedes paralysis and rarely occurs alone. It can manifest as tremulousness, obtundation, agitation, and autonomic dysfunction. The latter is recog-
nized by labile hypertension, hypotension, tachycardia, arrhythmias, and excessive sweating. There may be upper motor neuron (UMN) signs of spasticity and hyper-reflexia and Babinski signs (23). Muscle pains, muscle cramps, fasciculations, and radicular pain rarely occur without paralysis, but when they do, they usually precede paralysis by 24 to 48 hours. Paralytic disease is due to poliovirus infection of the motor neuron. Spinal cord anterior horn cells and other motor neurons are selectively vulnerable to poliovirus infection (24–27). Infection by poliovirus results in a variable distribution and variable extent of paralysis.

**Clinical Symptoms and Signs**

Paralytic poliomyelitis can be of bulbar, spinal, or bulbospinal types (28). Paralytic disease accounts for 0.1 to 2.0% of all poliovirus infections during an epidemic (22,29). Spinal paralytic poliomyelitis is the most common type. It affects the lower extremities more frequently than the upper, and paralysis is usually asymmetric, flaccid, patchy, and more proximal than distal (30). As paralysis progresses, reflexes are lost. Over several days, the other extremities may become paralyzed, and bulbar involvement may occur. Extension of paralysis is unlikely to occur 5 to 6 days after the onset of paralysis. Atrophy develops over several weeks. Rarely, a transverse myelitis with paraesthesia, urinary retention, sensory complaints and signs and autonomic dysfunction including hyperhidrosis or hypohidrosis, and decreased limb temperature may occur (31,32).

Bulbar or brainstem poliomyelitis occurs in 10 to 15% of paralytic cases (30). It can involve any of the cranial nerves and the medullary reticular formation. Affected adults usually have bulbospinal poliomyelitis, whereas children are more likely to have isolated bulbar involvement. The most frequently involved cranial nerves are the VIIth, IXth, and Xth, resulting in facial weakness and difficulty with swallowing and phonation. Reticular formation involvement can result in respiratory problems with ataxic breathing, lethargy and obtundation, and cardiovascular dysfunction including hypertention, hypotension, and cardiac arrhythmias (33).

Chronic or persistent poliovirus infection occurs infrequently in children with immunodeficiency who receive the live oral vaccine (34,35). The immunodeficiency is usually agammaglobulinemia, but infection also rarely occurs in those with cellular immunodeficiency usually several months after vaccination (34–36). The affected individual may present with lower motor neuron (LMN)
paralysis and progressive cerebral and intellectual dysfunction, with death in several months. Similar chronic infections have been caused by other enteroviruses (37).

Epidemiology

Incidence

The incidence of paralytic poliomyelitis peaked in the United States in 1952 with more than 20,000 cases (38). Because of the introduction of the killed IPV, or Salk vaccine, in 1954 and the live attenuated OPV, or Sabin vaccine, in 1961, the incidence has decreased to less than 10 cases per year in the United States (Fig. 2) (1,8,9,39). There is still a relatively high occurrence of the disease in Asia and Africa (40,41).

Transmission

Poliovirus is primarily spread by fecal-hand-oral transmission from one host to another. The virus is shed in oral secretions for several weeks and in the feces for several months (22,42). It is often introduced into the household by small children who are not toilet trained (43) and spreads in a family very rapidly, infecting most members in 4 to 5 days (42,44). Household spread depends on prior immunity, household size, and sanitary hygiene conditions (45). Transmission is related also to environmental factors such as sanitation, level of hygiene, crowded conditions, geography, the season, and host characteristics.

Endemic Versus Epidemic Activity

The geographic location and the accompanying temperature changes are factors that result in endemic or epidemic poliovirus activity. In tropical and semitropical areas, poliovirus circulates year around, the so-called endemic pattern, whereas in temperate zones, epidemics peak in the summer and early fall (45,46). From ancient times until the late 1800s, poliovirus activity was primarily endemic due to crowding, poor personal hygiene, and poor public sanitation (47,48). By early childhood, most individuals had been infected by all three types of poliovirus (49), and infrequently sporadic cases of paralytic poliomyelitis or true “infantile paralysis” were seen (50). This endemic pattern still occurs in semitropical and tropical underdeveloped areas of the world.

In the late 1800s, in developed temperate areas of the world, epidemic activity began to occur probably due to improved personal hygiene and public sanitation (2,51); accordingly, infants and small children were not previously exposed to poliovirus, creating a large pool of susceptible older children, adolescents, and adults. Because the latter are more likely to develop severe disease (3), when poliovirus infection sweeps through this virgin population, a high rate of paralysis can occur (22).

Predisposing Factors

There are other predisposing factors for paralytic poliomyelitis (3). Age is one factor; older children, adolescents, and adults have more severe and extensive paralysis and a higher incidence of death than infants and young children (52–54). Men and boys have a greater susceptibility to poliomyelitis (52,54). Tonsillectomy before or at the time of infection is associated with a higher incidence of bulbar involvement. Traumatic and injected extremities are more likely to become paralyzed.

![FIG. 2. Incidence of poliomyelitis in the United States, 1935–1964. (From Ref. 1, with permission.)](image-url)
the so-called provoking effect (55). Physical exertion predisposes to more severe paralysis, whereas pregnancy increases the incidence of paralytic disease by about threefold (56).

Pathology and Pathogenesis

As previously noted, polioviruses and other enteroviruses are spread by fecal-hand-oral transmission. After replication in the oropharynx and intestinal mucosa, the virus replicates in the submucosal lymphatic tissue (57), leading to a primary viremia, followed by replication in nonneural target tissues, and secondary viremia and CNS invasion. The exact route the poliovirus takes to enter the CNS is unclear, but viremia is required for CNS invasion (58,59). There is evidence to suggest that poliovirus enters the neuraxis at areas where the blood–brain barrier is defective, such as the area postrema (60). Another possibility is that the virus reaches the neuromuscular junction during the viremia, entering the distal axon and transported by retrograde axonal transport to the CNS (61–63). Poliovirus dissemination in the CNS occurs along nerve fiber pathways, probably by fast axonal transport (57,63,64).

Pathologic changes are seen several days after poliovirus infection of anterior horn cells. Initially, the Nissl substance shrinks and dissolves, leading to diffuse chromatolysis and loss of basophilic staining (6). If infection does not resolve at this point (65), nuclear shrinkage, eosinophilic type B inclusions, and cellular membrane disintegration occur. The inflammatory response consists of meningeal, perivascular, and parenchymal infiltrates, initially composed of polymorphonuclear leukocytes over the first 24 to 48 hours, followed by mononuclear and microglial cell responses with neuronophagia (25,66).

Laboratory Studies

General laboratory tests are uninformative. The complete blood count may reveal a peripheral leukocytosis. Cerebrospinal fluid (CSF) abnormalities are similar to those seen with many other CNS viral infections. The CSF cell count is increased, which initially may be a polymorphonuclear leukocytosis followed by a shift to mononuclear cells in 12 to 48 hours (3). At times it may be important to repeat the lumbar puncture to exclude bacterial infection. The cell count often reaches several hundred cells per mm³ but can be as high as several thousand. It usually declines precipitously within 2 weeks. Initially, the CSF protein is normal or mildly elevated but may rise to 100 to 300 mg/dL over several weeks and may remain high for months. Hypoglyccorrachia is rarely seen (3). Newer generation magnetic resonance imaging studies may show localization of inflammation to the spinal cord anterior horns (67). Virus isolation and serologic studies are needed to confirm the diagnosis.

Poliovirus can be isolated from the oropharynx for several weeks and from the stool for several months (22,68). It is almost never isolated from the CSF (69). Because several enteroviruses may be isolated from the stool, serologic testing is needed to confirm the responsible virus type. A fourfold or greater rise in serum antibody titer between the acute and convalescent specimens is considered diagnostic. It is important to obtain the acute phase specimen as soon as possible to detect the fourfold rise. The convalescent phase sample should be obtained at least 2 weeks, and preferably 4 weeks, after the acute phase specimen is obtained. A CSF/serum antibody ratio of greater than 1:150 may also be diagnostic (70), as well as CSF IgM antipoliovirus antibody (71).

Differential Diagnosis

The combination of fever, headache, stiff neck, and asymmetric flaccid paralysis without sensory loss, and a CSF profile consistent with viral infection make paralytic poliomyelitis likely. The diagnosis may be difficult if these major manifestations are lacking or if unusual manifestations, such as urinary retention or sensory loss, occur. Nonpolio enteroviruses can also cause polio-like paralysis, although it is usually not as severe as that seen with poliovirus (3,72). Several other viruses can occasionally cause acute LMN paralysis, especially rabies (73) and herpes zoster (74). Other disease processes in the differential include transverse myelitis, acute spinal cord compression from epidermal abscess, Guillain–Barré syndrome, acute intermittent porphyria, toxic neuropathies, and botulism (69,72,75).

Management

Treatment

Treatment for paralytic poliomyelitis initially relies on supportive care followed by passive and then active physical therapy and orthopedic measures. Bedrest is recommended during the preparalytic stage because physical exercise can increase the severity of paralysis (3). Treatment of sore muscles with hot packs, fever with analgesics, and anxiety with anxiolytics may be calming. In addition, acute paralysis should be treated with hospitalization, appropriate positioning with splints to prevent contractures, foot boards to prevent foot drop, and frequent turning to prevent decubiti (69). Patients with bulbar involvement generally require fluid and electrolyte support (76). During the convalescent period, active physical therapy with nonfatiguing muscle-strengthening exercises and hydrotherapy may be beneficial. Braces and other orthoses may be needed for weak muscles or severe extremity paralysis. Arthrodesis, tendon transfers, leg-shortening procedures, and other orthopedic surgery
interventions should be deferred for 1.5 to 2 years after maximum recovery has occurred (77,78).

**Prevention**

Vaccination is the mainstay of prevention. The injectable killed IPV and the live attenuated OPV have been very effective in decreasing the incidence of poliomyelitis (1,38). The advantages and disadvantages of each vaccine have been extensively debated (3,45). The killed vaccine results in relative short-term immunity of 5 to 10 years, necessitating frequent revaccinations, but it does not cause paralysis. A very high level of vaccination of the population is required with the killed vaccine to prevent the spread of wild-type virulent viruses in the community. In contrast, the live vaccine is effective in producing long-term immunity, possibly lifelong, producing immunity by exposure to vaccine strains circulating in the population (secondary spread) (79) and eliminating the circulation of wild-type virulent strains. However, the live vaccine rarely causes paralysis (55,80). Recently in the United States, the recommendations for vaccination have been changed to a sequential vaccination schedule of two doses each of the IPV followed by the OPV (81). Prevention can also occur by stopping the spread of infection through the use of good personal, family, and public hygiene. Handwashing and the use of clean utensils can decrease person-to-person fecal-handoral transmission (43). Adequate water and sewage treatment can decrease the spread of poliovirus (82).

**Prognosis and Complications**

With good supportive care, especially for respiratory insufficiency, death from paralytic poliomyelitis occurs in only 7 to 8% of patients (69). Death is usually the result of bulbar involvement with respiratory and cardiovascular impairment. Patients who survive an acute attack of paralytic poliomyelitis usually have significant recovery of motor function, although permanent and severe residual paralysis of one or two extremities is not uncommon. Motor improvement usually starts within weeks after onset, although in rare cases, extension of localized paralysis can be seen as late as the third or fourth week of illness (83). About a 50% recovery occurs in 3 months, and 75% in 6 months. Minimal further improvement occurs slowly over the next 2 years (84).

Acute and subacute complications include those related to immobility, such as decubiti, contractures, foot and wrist drop, and urinary tract infections. Pneumonia can result from bulbar muscle dysfunction and respiratory insufficiency. More chronic complications include osteoporosis, skeletal deformities such as scoliosis, reduced extremity growth, and PPS, discussed in the following section, which generally occurs 30 to 40 years after acute polio.

**POST-POLIO SYNDROME**

**History**

New muscle weakness as a late sequel of poliomyelitis was initially recognized by Charcot and others in 1875 (85–87). Between 1875 and 1975, about 200 cases were reported in the world’s literature (23,88). Since 1975, a large “epidemic” of several thousand cases has occurred (23,89,90). They relate to the large epidemics of poliomyelitis that occurred during the first half of this century (reviewed in Ref. 91). Since our last in-depth review of this topic (91), recent advances have centered on the pathophysiology, etiology, and treatment of the muscle weakness. The generalized nonspecific manifestations and sympathetic and UMN involvement in poliomyelitis and PPS, including the epidemiology, muscle biopsy findings, etiologic hypotheses, symptomatic treatment, and management, have been previously reviewed by Jubelt and colleagues (23,91).

**Clinical Manifestations**

**Definition of the Syndrome**

PPS is a neurologic disorder that produces a cluster of symptoms in individuals who had acute paralytic poliomyelitis usually 30 to 50 years earlier. They commonly include progressive weakness, fatigue, and pain of muscles and/or joints and less commonly muscle atrophy, breathing and swallowing difficulties, sleep disorders, and cold intolerance. Some symptoms such as weakness, muscle fatigue, atrophy, and maybe generalized fatigue appear to be caused by a progressive degeneration or dysfunction of motor units and eventually motor neurons. Other symptoms such as joint pain are more likely the result of excessive wear and tear on different parts of the musculoskeletal system.

Because some of the manifestations, especially fatigue, are nonspecific, the syndrome itself can be hard to diagnose unless other musculoskeletal or neurologic components are present. Fatigue is the most common manifestation overall (89,91,92), but new weakness, sometimes accompanied by atrophy, is the signature for the neurologic disorder termed “post-polio progressive muscular atrophy” (23,89). The criteria for PPS now used by most investigators and clinicians in the field were first described by Mulder et al. (93): documentation of paralytic polio, partial recovery of function followed by a period of stabilization, and progressive neurologic deterioration (Table 1). The musculoskeletal manifestations, mainly joint and muscle pain, result from the combination of long-term residual weakness and the stress in joints, ligaments, and tendons.

**Neurologic Manifestations**

Fatigue is clearly the most prominent manifestation, occurring in up to 80% of patients (23,89,90,92) (Table 2).