TABLE 1. Diagnostic criteria for post-polio syndrome* 

1. A prior episode of paralytic poliomyelitis with residual motor neuron loss (which can be confirmed through a typical patient history, a neurologic examination, and, if needed, an electrodiagnostic exam).
2. A period of neurologic recovery followed by an interval (usually 15 years or more) of neurologic and functional stability.
3. A gradual or abrupt onset of new weakness or abnormal muscle fatigue (decreased endurance), muscle atrophy, or generalized fatigue.
4. Exclusion of medical, orthopedic, and neurologic conditions that may be causing the symptoms mentioned in 3.

*Consensus of the Post-Polio Task Force.

It is generally described as a disabling generalized exhaustion, the “polio wall,” that follows even minimal physical activity (94). Their fatigue also has been described by patients as “increasing physical weakness,” “tiredness,” “lack of energy,” and “increasing loss of strength during exercise” (95); thus, it can either be perceived as generalized or muscular in origin (94,96). The fatigue can also affect mental as well as physical functioning, such as when it is severe patients find it difficult to concentrate or collect their thoughts and appear confused (95). It may be improved by decreasing physical activity, pacing daily activities, and taking frequent rest periods and naps (96,97). PPS fatigue appears to respond better to sleep than that of the chronic fatigue syndrome, although frequent rest periods are also helpful.

The pathophysiology of fatigue is not clear. Bruno et al. (98) hypothesized that the age-related attrition of neurons in the substantia nigra and possible degeneration of reticular formation neurons, combined with the already decreased number of these neurons resulting from poliomyelitis, might cause impairment of the brain activating system. Others have related the fatigue to diffuse deterioration of the motor unit at the neuromuscular junction (97,99). Some PPS patients, 10 to 20%, have muscle fatigability reminiscent of myasthenia gravis (100), as similarly reported in amyotrophic lateral sclerosis (101). A number of medications can be used to treat the generalized fatigue as indicated below. One study found that neuromuscular junction transmission, as measured by jitter on single-fiber electromyography (SFEMG), improved with anticholinesterase treatment in up to 50% of PPS patients so studied, and 50% also experienced decreased general fatigue and muscle fatigability (102). A recently completed controlled double-blind trial of pyridostigmine in PPS was, however, negative (personal communication).

New slowly progressive muscle weakness is the most important neurologic problem, occurring in most affected patients (90,91,103) (Table 2). It appears to be related to a disintegration of the LMN unit (104,105) and can occur in muscles previously affected and partially or fully recovered or in unaffected muscles (90,91) (Table 2). Human electromyography (EMG) (106) and animal studies (107,108) indicate that some clinically unaffected muscles were involved subclinically during the acute poliomyelitis, but previously affected muscles were more likely than unaffected muscles to later become weak (90,91) (Table 2). The distribution of the new weakness, which is usually asymmetric, proximal, distal, or patchy, appears to correlate with the severity of paralysis at the time of the acute poliomyelitis and with the amount of recovery and thus with the number of surviving motor

TABLE 2. Most common new late manifestations of poliomyelitis in patients referred to post-polio clinics* 

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Houston* (n=132)</th>
<th>Madison| (n=79)</th>
<th>(n=100)</th>
<th>(n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>89%</td>
<td>86%</td>
<td>83%</td>
<td>86%</td>
</tr>
<tr>
<td>Joint pain</td>
<td>71%</td>
<td>77%</td>
<td>72%</td>
<td>73%</td>
</tr>
<tr>
<td>Muscle pain</td>
<td>71%</td>
<td>86%</td>
<td>74%</td>
<td>73%</td>
</tr>
<tr>
<td>Weakness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previously affected muscles</td>
<td>69%</td>
<td>80%</td>
<td>88%</td>
<td>88%</td>
</tr>
<tr>
<td>Previously unaffected muscles</td>
<td>50%</td>
<td>53%</td>
<td>61%</td>
<td>59%</td>
</tr>
<tr>
<td>Total*</td>
<td>—</td>
<td>87%</td>
<td>95%</td>
<td>90%</td>
</tr>
<tr>
<td>Atrophy</td>
<td>28%</td>
<td>39%</td>
<td>59%</td>
<td>52%</td>
</tr>
<tr>
<td>Cold intolerance</td>
<td>29%</td>
<td>39%</td>
<td>49%</td>
<td>53%</td>
</tr>
<tr>
<td>Respiratory insufficiency</td>
<td>—</td>
<td>39%</td>
<td>42%</td>
<td>36%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>—</td>
<td>30%</td>
<td>27%</td>
<td>36%</td>
</tr>
</tbody>
</table>

*Modified from Ref. 91.

**Adapted from Ref. 90. All patients met criteria for PPS.

\Adapted from Ref. 92. All patients had histories and examinations compatible with diagnosis of previous poliomyelitis.

First 200 patients with histories and examinations compatible with diagnosis of previous poliomyelitis.

Total percent of patients with new weakness.
neurons (6,104,109). New atrophy does not occur as an isolated manifestation and is seen in fewer than half of patients with new weakness (90,110). In addition to the weakness and atrophy caused by the disintegration of the motor unit, rarely UMN signs can occur (23). They include hyperreflexia, Babinski signs, and occasionally spasticity. Of 180 PPS patients so studied, we found UMN signs in 15 (8.3%), 7 of whom underwent myelography or magnetic resonance imaging of the spinal cord to exclude compression (23). This percentage is very similar to the frequency of UMN signs found during acute poliomyelitis (23). Muscle pain or myalgia, which also occurs in most patients (90,91,103) (Table 2), appears to be due to overuse of weak muscles. Similar symptoms occur in overused weakened muscles in other neuromuscular diseases (23). The pain is a soreness or aching feeling that occurs with minimal exercise. A small number of patients can have muscle tenderness on palpation. Rest, braces, splints, and anti-inflammatory medications may be beneficial.

New muscle weakness may also involve specific muscles groups, causing respiratory insufficiency, bulbar muscle weakness, and sleep apnea. Respiratory insufficiency primarily occurs in patients with severe residual respiratory impairment with minimal reserve (111,112). Similar to limb weakness, respiratory failure is more likely to occur in patients who required respiratory support during the acute disease and hence had more severe disease and in those that contracted polio at an age older than 10 years (111). Patients with PPS and chronic respiratory failure lose an average of 1.9% of their vital capacity per year (113). It is usually due to respiratory muscle weakness but also to central hypoventilation because of the residual damage from earlier bulbar poliomyelitis (33). Other factors such as pulmonary or cardiac disease or scoliosis may contribute to the problem. Initially, respiratory failure begins with nocturnal alveolar hypoventilation, and patients may require only nighttime respiratory support (114). If already on nighttime respiratory support, they may eventually require total ventilator support (115). Bach (116) studied 145 post-polio myelitis individuals who were managed by noninvasive alternatives to tracheostomy. Mouthpiece intermittent positive pressure ventilation, nasal intermittent positive pressure ventilation, manually and mechanically assisted coughing, and noninvasive blood gas monitoring in the home were the main techniques used for optimizing quality of life and for avoiding complications. With the use of these measures, acute respiratory failure and tracheal intubation were generally avoided.

Bulbar muscle weakness is now also a recognized component of PPS (117), of which dysphagia is the most common problem. Residual dysphagia occurs in 10 to 20% of polio survivors (118). It is primarily due to pharyngeal and laryngeal muscle weakness; however, local pharyngeal or esophageal problems should also be excluded. Some patients complain of food sticking, making swallowing slow or difficult, often with coughing and choking (118). Videofluoroscopic studies may reveal impaired tongue movements, delayed pharyngeal constriction, pooling in the valleculae or piriform sinuses, and rarely aspiration, which is usually mild (117). Infrequently, other bulbar muscles, such as the facial muscles and vocal cords, may become weaker in PPS (119); dysarthria has also been reported (23).

Sleep apnea is not an uncommon problem in post-polio patients. It may be central, obstructive, or mixed (120,121). Most patients with central sleep apnea have a history of bulbar polio, and some required ventilatory support (120). It is probable that residual damage to the brainstem reticulum formation predisposes to central sleep apnea. In comparison, obstructive sleep apnea appears to be related to pharyngeal muscle weakness, obesity, and musculoskeletal deformities (121). Respiratory muscle weakness may also contribute to sleep apnea (122).

Fasciculation and cramps without weakness, muscle pseudohypertrophy, and tingling paresthesias are other neuromuscular problems that may occur in post-polio patients, with or without new weakness (23).

Musculoskeletal Manifestations

Pain from joint instability is the major musculoskeletal problem and can occur without new weakness. The long-term over stressing of joints because of residual weakness eventually results in joint deterioration. Progressive scoliosis, poor posture, unusual mechanics because of deformed joints, uneven limb size, failing tendon transfers, and failing joint fusions can all contribute to joint pain. It can also arise from over stressed tendons due to joint deformities or because of long-standing muscle weakness. These joint problems frequently lead to loss of mobility and a return to using old assistive devices (123). Compressive radiculopathies and mononeuropathies may occur as secondary musculoskeletal complications (23,124).

Other Manifestations

Other symptoms much less frequently reported include increased sleep requirements, cold intolerance, and psychologic stresses (23,90). Increased sleep requirements probably relate to severe fatigue. Many PPS patients complain of cold intolerance (90) (Table 2). They report worsening symptoms, including increasing generalized fatigue and weakness when exposed to cold temperatures (125). Patients may also develop coolness and color changes such as cyanosis and blanching of the affected extremity that relate to sympathetic intermediolateral column damage during prior acute poliomyelitis (126). Psychological symptoms, related to the reemergence of a supposedly old resolved problem and to the stresses of
the required major changes in lifestyle, can be overwhelming at times (127,128).

Epidemiology

Prevalence

Data regarding the incidence and prevalence of PPS is quite variable. Cordy et al. (103) found a prevalence of PPS of 22.4% in those with previous poliomyelitis, but a repeat study from the same institution found a prevalence of 64% (129). The 1987 National Health Interview Survey estimated that about half of the 1.63 million people in the United States who survived acute poliomyelitis had new late effects (PPS) (130). Another study from 1987 found a frequency of 42% (131). Ramlow et al. (132) detected a prevalence of 28.5% among all cases of paralytic poliomyelitis. The variation in prevalence appears to relate to the definition of PPS. About 50 to 64% of patients have new problems, but only about 20 to 30% have new progressive weakness. A large number of cases are seen because of the large epidemics of poliomyelitis that occurred in the United States in the 1940s and 1950s (23).

Delay in Onset of Post-Polio Syndrome

The delay in onset between acute poliomyelitis and PPS ranges from 8 to 71 years in various series (23). The more severe the acute polio, the earlier new symptoms are likely to occur (94). In various series the average interval is about 35 years (23,94,132,133).

Risk Factors

Several risk factors predispose to the development of PPS. One is the severity of the polio and resulting paralysis (94,129,134,135); another is the age at onset of the poliomyelitis. Acute poliomyelitis in adolescents and adults is more severe than in infants and small children (23), and the former patients are more likely to develop PPS (94,109). Another risk factor is the amount of recovery; the greater the recovery, the more likely PPS will occur (109), suggesting that reinnervation is unable to be maintained 30 to 40 years later. In those who do recover totally or partially, excessive exercise or overuse appears to predispose them to PPS (109,135).

Course of Post-Polio Progressive Muscular Atrophy

It is difficult to measure the course of many PPS manifestations; however, weakness lends itself to objective analysis. Mulder et al. (93) reported continuous progression of weakness during the 12 years of follow-up. Dalakas et al. (136) used Medical Research Council grading and noted stepwise or steady progression of weakness at an average rate of only 1% per year over a mean follow-up period of 12.2 years. Some studies with shorter follow-up periods of 2 (137), 2.5 (138), and 5 years (139) did not demonstrate progression of the weakness; however, two other studies (140,141), each with 4-year follow-up periods, found a rate of progression of 2% per year. Many patients have a stepwise course with plateaus, and progression may be difficult to demonstrate unless the follow-up period is of adequate duration, generally greater than 5 or even 10 years. Significant objective clinical weakening was noted by others (142), including weakness of bulbar musculature (117).

Laboratory Studies

Routine blood tests, including erythrocyte sedimentation rate, are normal except for the creatine kinase (CK), which may be mildly elevated (23,129,143,144). In one study, an increased creatine kinase level was more likely to occur in those with progressive weakness (129), and markedly elevated values probably indicate muscle overuse (145). In most studies, CSF parameters have been normal, although a mildly elevated protein content has been seen (23).

Electromyography

In 1987 (23), we analyzed EMG studies in 26 patients with old poliomyelitis. Concentric needle EMG of patients with old polio showed chronic denervation and reinnervation including abnormally increased motor unit potential amplitude, duration, and polyphasia and decreased interference patterns both in patients and in muscles with or without new weakness, tested years after acute polio, and in muscles that were clinically uninvolved during the acute disease. Active new denervation including fibrillation and positive sharp wave activity was usually of a mild degree (Table 3) and seen in some PPS patients with new weakness (range, 0 to 45%) but also in those without new weakness. Fasciculation was seen more frequently than acute denervation. Nerve conduction velocities were also generally normal. SFEMG revealed increased fiber density and the neuromuscular transmission defects of increased jitter and blocking (Table 3). The number of motor units with abnormal jitter and neuromuscular blocking correlated with the number of years since acute poliomyelitis (146). EMG and SFEMG studies, however, did not discriminate PPS from the asymptomatic cases (104). Wiechers (147) has been the only one to analyze macro-EMG and showed that large reinnervated motor units decreased with time from recovery of the acute disease, suggesting a loss of terminal sprouts.

It now appears that the enlarged motor units that develop by collateral sprouting after acute poliomyelitis never fully stabilize (148). There may be continuous denervation and reinnervation, with denervation becoming more prominent later in life as reinnervation becomes
less efficient. Progressive weakness appears to be the “end of the spectrum of all post-polio myelitis patients” (149). Similar to clinical studies suggesting that good recovery is a major risk factor for PPS (109), SFEMG studies reveal a positive correlation between increased jitter and fiber density. They also suggest that muscles with enlarged motor units due to sprouting or recovery are more likely to become unstable later in life (110,150). Spontaneous activity, like jitter and blocking, appear to be more frequent in symptomatic muscles (151,152). Macro-EMG motor unit potential amplitudes are increased in post-polio muscles (141,153). In some muscles, the macro-EMG amplitudes may decrease in size as motor neurons die (154), whereas in others, it may increase as other motor neurons compensate (141). Despite the fact that EMG studies cannot be used to diagnose PPS because symptomatic and asymptomatic muscles have the same findings, the aforementioned studies have contributed greatly to our understanding of the pathophysiology of neuromuscular junction dysfunction after acute poliomyelitis. EMG studies can also exclude other diagnoses and determine the extent of the old acute poliomyelitis (155).

**Muscle Biopsy**

The biopsy findings of patients with old poliomyelitis reveal evidence of chronic denervation, reinnervation, and active denervation (23). The primary sign of chronic denervation and reinnervation is fiber type grouping. A sign of active denervation is the presence of small angulated fibers that arise with terminal sprout denervation; group atrophy, sometimes seen in amyotrophic lateral sclerosis, is an infrequent finding in PPS. The expression of neural-cell adhesion molecules on the surface of muscle fibers is another finding that suggests active denervation (104,105). Unfortunately, chronic denervation and reinnervation and acute denervation have been seen in both symptomatic and asymptomatic post-polio patients, and muscle biopsies cannot clearly distinguish between them. Dalakas (156) found that originally affected muscles that had partially recovered had a variable degree of chronic and acute neurogenic atrophy or fiber-type grouping, with variable group atrophy and angulated fibers in some, combined with secondary myopathic features. Muscles originally affected that had fully recovered also showed signs of both chronic fiber-type grouping and recent denervation or angulated fibers, with few secondary myopathic features. Muscles originally spared clinically but newly symptomatic had signs of chronic denervation and reinnervation and recent denervation, but secondary myopathic features were minimal or absent. Asymptomatic post-polio patients had signs of chronic denervation and reinnervation but no signs of acute denervation or myopathy. These findings need to be confirmed in a larger sampling. The significance of the occasional findings of classic myopathic features (156,157) and lymphocytic infiltrates (156) remains unclear.

**Etiology**

Jubelt and Cashman (23) outlined nine possible mechanisms for the development of PPS (Table 4). Over the last 10 years, enough information has accumulated that the possibilities can now probably be narrowed even more. Normal aging alone cannot explain the development of PPS. The loss of anterior horn cells and motor neurons...