

# Management of postpolio syndrome

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Postpolio syndrome is characterised by the exacerbation of existing or new health problems, most often muscle weakness and fatigability, general fatigue, and pain, after a period of stability subsequent to acute polio infection. Diagnosis is based on the presence of a lower motor neuron disorder that is supported by neurophysiological findings, with exclusion of other disorders as causes of the new symptoms. The muscle-related effects of postpolio syndrome are possibly associated with an ongoing process of denervation and reinnervation, reaching a point at which denervation is no longer compensated for by reinnervation. The cause of this denervation is unknown, but an inflammatory process is possible. Rehabilitation in patients with postpolio syndrome should take a multiprofessional and multidisciplinary approach, with an emphasis on physiotherapy, including enhanced or individually modified physical activity, and muscle training. Patients with postpolio syndrome should be advised to avoid both inactivity and overuse of weak muscles. Evaluation of the need for orthoses and assistive devices is often required.

## Introduction

12–20 million people worldwide have sequelae of poliomyelitis, according to Post-Polio Health International. Postpolio syndrome is the most common neuromuscular disorder in Sweden<sup>1</sup> and the most prevalent motor neuron disease in the USA.<sup>2</sup>

A common misconception is that people in developed countries who have had poliomyelitis are old. Large epidemics were frequent in Europe and in the USA in the 1940s and during the first half of the 1950s when vaccination programmes were launched,<sup>2,3</sup> and many people who have recovered from poliomyelitis infection are still of working age. A global eradication of poliomyelitis is close to accomplishment; in a few years time there should be no new cases of the disorder. However, in several developing countries, many young people have recently contracted the disease. Although the number of people with sequelae of poliomyelitis will decrease in Europe and the USA in the next few decades, many people in developing countries will be affected for at least a generation.

Many health-care workers believe that the sequelae of poliomyelitis do not change throughout a patient's lifetime. However, more than a century ago the development of new or exacerbated symptoms was already reported long after the acute poliomyelitis infection.<sup>4</sup> The existence of postpolio syndrome has been questioned, but the late effect of poliomyelitis, or postpolio syndrome, is generally accepted as a defined clinical entity.<sup>2,5,6</sup> The prevalence of postpolio syndrome has been reported to be between 20% and 85% of people who have had poliomyelitis.<sup>2,6,7</sup> This disparity is most probably caused by the use of different clinical diagnostic criteria. In this context, it is important to remember that people who have sequelae of poliomyelitis but who do not fulfil diagnostic criteria for postpolio syndrome might still have substantial loss of motor function and be in need of therapeutic interventions.

Interest in postpolio syndrome has increased over the past two to three decades, with research varying in focus from molecular to clinical aspects, and health-related quality of life. In this Review, we provide a comprehensive

summary of the pathophysiology and clinical characteristics of postpolio syndrome, outline diagnostic and treatment options, and suggest future research strategies.

## Pathophysiology

Studies of motor units of patients with postpolio syndrome have revealed an ongoing denervation–reinnervation process.<sup>8,9</sup> This is probably initiated after the acute poliomyelitis, and over time leads to increased motor unit areas caused by collateral sprouting of adjacent motor neurons in the spinal cord in patients with postpolio syndrome; a process also evident during normal ageing, although not until the seventh decade of life.<sup>10</sup> The motor unit area might increase by up to 20 times, reaching a level at which further reinnervation is no longer possible. Uncompensated denervation causes atrophy of muscle fibres and subsequently loss of muscle strength.<sup>8,9</sup> The underlying cause of the ongoing denervation resulting in the motor symptoms of postpolio syndrome is unclear. Several hypotheses have been proposed, as described below.

### Stress or overuse of motor units

Stress is a favoured hypothesis, proposed by Wiechers and Hubbell,<sup>11</sup> which attributes postpolio syndrome to degenerating terminal axonal sprouts and an inability to maintain the increased metabolic demand from the enlarged motor unit. Overuse was suggested by Perry and colleagues<sup>12</sup> in 1988. Overuse of remaining motor units leads to activation of compensatory mechanisms: muscle fibre transition from fast to slow contracting muscle fibres and muscle fibre hypertrophy, that is, changes in contractile properties of the overused muscle fibres and an increase of the contractile tissue.<sup>8,13–15</sup> Compensatory changes in the muscle have negative effects, such as muscle pain and fatigue caused by lower capillarisation and changes in the contractile properties of the remaining muscle fibres. These changes favour muscle strength before endurance,<sup>15</sup> and thus a discrepancy between low energy resynthesis and a high energy utilisation in the overused muscle fibres, which is

of importance for development of fatigue, was assumed. Nonetheless, results from longitudinal studies do not show that overuse leads to increased persistent muscle weakness.<sup>16</sup>

### Ageing

The length of time between acute poliomyelitis and the start of symptoms is a risk factor for postpolio syndrome,<sup>17</sup> and two studies independently concluded that age was a confounding factor for the development of postpolio syndrome.<sup>17,18</sup> However, the normal ageing process can also cause muscle weakness in patients with postpolio syndrome.<sup>16</sup>

### Persistent virus

Persistence of poliovirus fragments might cause postpolio syndrome. Mutated poliovirus genomic sequences have been detected in the CSF of some patients,<sup>19,20</sup> but not in the CSF of others.<sup>21</sup> One study<sup>22</sup> reported detection of poliovirus genome fragments in all patients with postpolio syndrome. Further study is clearly needed to prove the hypothesis of a persistent viral infection in postpolio syndrome.

### Immunological factors and chronic inflammation

Increasing interest in recent years has been devoted to the immunological process underlying postpolio syndrome. Inflammatory changes have been described in the spinal cord<sup>23,24</sup> and the CSF<sup>25</sup> of patients with postpolio syndrome. Also, concentrations of several cytokines, mainly those with proinflammatory actions (eg, interferon- $\gamma$  and tumour necrosis factor [TNF]), are high in the CSF of patients.<sup>26–28</sup> These findings probably reflect chronic inflammation in the spinal cord parenchyma, with potential damage to motor neurons. Further support for this scenario was obtained by use of unbiased proteomics of the CSF. A small series of proteins and their fragments were found at high concentrations in the CSF only in patients with postpolio syndrome; the peptides were all involved in apoptosis and inflammation.<sup>29</sup> Furthermore, peptide cleavage patterns were consistent with actions of TNF. A systemic proinflammatory response in postpolio syndrome is also likely. High TNF concentrations in blood were associated with increased muscle pain.<sup>30</sup> The finding of high titres of poliovirus antibodies and high numbers of regulatory T cells<sup>31</sup> further supports the notion of an active immunological process.

The role of this chronic inflammation in postpolio syndrome is unclear and further study is needed. Potential causes include a late aberrant immune response to the original infection, a persistent immune response, or persistence of viral particles (boosting of the response by non-polio enteroviruses might also be involved); a late autoimmune complication of the original infection; and an immune response secondary to ongoing neurodegeneration caused by other factors.

### Panel: Criteria for postpolio syndrome<sup>16</sup>

- 1 Prior paralytic poliomyelitis with evidence of motor neuron loss, as confirmed by history of the acute paralytic illness, signs of residual weakness and atrophy of muscles on neurological examination, and signs of denervation on electromyography.
- 2 A period of partial or complete functional recovery after acute poliomyelitis, followed by an interval (usually 15 years or more) of stable neurological function.
- 3 Gradual or sudden onset of progressive and persistent new muscle weakness or abnormal fatigability (decreased endurance), with or without generalised fatigue, muscle atrophy, or muscle and joint pain. (Sudden onset may follow a period of inactivity, or trauma or surgery.) Less commonly, symptoms attributed to postpolio syndrome include new problems with breathing or swallowing.
- 4 Symptoms persist for at least a year.
- 5 Exclusion of other neurological, medical, and orthopaedic problems as causes of symptoms.

If the neurodegeneration in postpolio syndrome is an ongoing process caused by chronic inflammation, treatment of the disorder with drugs that modify the immune response (eg, intravenous immunoglobulin and cortisone, as discussed later) should be possible.

### Genetics

Some studies have attempted to find a genetic background to postpolio syndrome. Bartholdi and colleagues<sup>32</sup> reported that the *SMN* gene deletion, a cause of adult spinal muscular atrophy, was not present in patients with postpolio syndrome. Polymorphisms in the Fc-gamma receptor IIIA might be a risk factor for postpolio syndrome.<sup>33</sup> Further studies of possible gene variants that could predispose to both acute poliomyelitis and postpolio syndrome would be of interest.

### Diagnosis

Several diagnostic criteria for postpolio syndrome have been proposed.<sup>8,34–36</sup> Different criteria from different countries focus on muscle atrophy<sup>34</sup> or muscle dysfunction,<sup>10</sup> but all are mainly based on those originally suggested by Halstead and Rossi.<sup>36</sup> In 1991, Halstead added gradual or abrupt onset of new neurogenic muscular weakness as a criterion.<sup>37</sup> In the criteria suggested by the 29th European Neuromuscular Centre workshop on postpolio muscle dysfunction, clinical and neurophysiological findings, MRI, or both, compatible with a lower motor neuron lesion were included.<sup>8</sup> At the March of Dimes international conference on postpolio syndrome in 2000, diagnostic criteria were recommended, including a criterion that symptoms should persist for at least 1 year (panel).<sup>16</sup>

Diagnosis of postpolio syndrome is based on clinical symptoms and signs (tables 1 and 2). To diagnose a patient with postpolio syndrome not all symptoms and signs

	Symptoms	Treatment
Muscle weakness	Further weakness in previously weak musculature or new weakness in previously clinically unaffected muscle groups	Physical activity, muscle training, avoiding muscle overuse and disuse, and lifestyle changes
Pain	Nociceptive pain Neurogenic pain	Symptomatic medication, physiotherapy, bracing, weight reduction Decompression and pharmacological treatment for neuropathic pain
Fatigue	Most often of physical character with decreased muscular endurance. Mental fatigue can also occur, that is, brain fatigue or decreased mental endurance	Physical activity, muscle training, rest, avoiding muscle overuse and disuse, lifestyle changes, weight reduction, and, if required, medication for restless legs syndrome, depression, and sleep disturbances
Hypoventilation	Caused by weakness of respiratory muscles and chest wall deformities, obstructive apnoea, and central apnoea	Assisted ventilation and inspiratory muscle training Invasive controlled mechanical ventilation
Dysphagia and dysphonia	Caused by weakness in oesophageal and laryngeal muscles	Instruction on swallowing and voice therapy

**Table 1: Symptoms and treatment of postpolio syndrome**

	Clinical signs	Investigation
Muscle function	Weak or no muscle strength. Lower motor neuron lesion with flaccid paralysis	Clinical examination Neurophysiology (electromyography) MRI
Tendon reflexes	Weak or no tendon reflexes in affected muscle groups	Clinical examination
Sensory function	No sensory loss, cold intolerance might be present	Clinical examination Neurophysiology (nerve conduction velocity)
Cranial nerves	Most often normal but might be impaired (bulbar poliomyelitis)	Clinical examination Investigation on oesophageal and laryngeal muscle function
Pulmonary function and sleep-disordered breathing	Weak respiratory muscles, chest wall and spinal deformities Daytime sleepiness	Pulmonary investigation, including complete spirometry Polysomnography

**Table 2: Clinical signs of postpolio syndrome**

need to be present. As stated previously, this is a diagnosis based on exclusion. The most common symptom of postpolio syndrome is a triad of fatigue, deterioration in muscle strength, and pain (panel). Serum creatine phosphokinase concentrations are usually normal.<sup>2,3</sup> Diagnosis is supported by electrophysiological examination including electromyography (EMG), which usually reveals longstanding neurogenic signs. Macro-EMG can enable a more precise quantification of remaining motor units and their size, thereby indicating the extent of the denervation and reinnervation process.<sup>38</sup>

Patients who had non-paralytic polio and those with clinically unaffected muscles and a history of poliomyelitis might present with postpolio syndrome and neurophysiological signs of denervation.<sup>39,40</sup> In people aged 60 years or over, loss of half of their motor units might not be associated with a decline in muscle strength;<sup>41</sup> this could explain both why paresis might not be recognised and the occurrence of new postpolio syndrome symptoms in extremities that were thought not to have been affected by poliomyelitis.

In a large cohort of patients with a reported history of poliomyelitis, 5% had normal EMG.<sup>42</sup> Sandberg and Stålberg<sup>42</sup> suggested that, despite normal EMG, there was a transient functional loss without degeneration of anterior horn cells, making these cells more vulnerable to later functional impairment.

### Symptoms and signs

Because poliomyelitis affects the anterior horn cells in the anterior part of the spinal cord (the first part of the motor unit), postpolio syndrome is a lower motor neuron disorder. The symptoms in patients with postpolio syndrome are muscle weakness and atrophy, and fatigue and pain from muscles and joints (table 1).<sup>2,37</sup> Other symptoms include cold intolerance, difficulty swallowing, muscle twitching and cramps, respiratory distress, and voice changes.<sup>2,3,7,17,37</sup>

On clinical investigation, signs of a lower motor neuron disorder are apparent; the most typical is asymmetrical flaccid paresis. Sensory deficits are not observed unless a secondary disorder is present, for example compression neuropathy (table 2).

Health-related quality of life has been investigated in patients with postpolio syndrome in several studies. Different questionnaires, mainly the SF-36<sup>43-46</sup> and the Nottingham health profile,<sup>47-51</sup> have been used. But, although different questionnaires were used, results were comparable, with low health-related quality of life in physical domains, pain, and vitality; however, results from mental domains are similar to those reported by control individuals. Patients with postpolio syndrome can have a high degree of independence with regard to personal activities of daily living but typically have difficulty with mobility.<sup>52-54</sup> Overall morbidity is high in patients with postpolio syndrome compared with that in healthy control individuals.<sup>55</sup> Besides, comorbidity and ageing can cause further health problems in these patients.<sup>44</sup>

### Muscle weakness and atrophy

In patients with postpolio syndrome new or increased muscle weakness and atrophy can be permanent, because of loss of motor units, or transient, because of muscle fatigue.<sup>2</sup> Progression of muscle weakness is probably slow but faster than in normal ageing.<sup>56</sup> Stolwijk-Swüste and colleagues<sup>57</sup> systematically analysed studies assessing the course of functional status and muscle strength over time in patients with postpolio syndrome. Only two studies that assessed functional status were of sufficient quality but they reported inconsistent results. Four studies that assessed muscle strength were of sufficient quality: two reported a decline in muscle strength and two reported no change. Grimby and colleagues<sup>58</sup> reported a decrease of muscle cross-sectional area in patients with poliomyelitis sequelae during a 4-year follow-up period<sup>58</sup> and a 9–15% decrease in muscle strength during a follow-up period of 8 years.<sup>9</sup> We recorded a 6% decrease in muscle power in a

selected muscle in patients with postpolio myelitis over a 6-month period.<sup>43</sup> McComas and colleagues<sup>59</sup> described a decrease in motor units of 13·4% in patients with previous poliomyelitis during a 2-year follow-up. Lower figures were reported by Sorenson and coworkers,<sup>60</sup> with a yearly loss of 3% during a 15-year follow-up period, and Ivanyi and colleagues<sup>61</sup> reported no decrease of muscle strength during a follow-up period of about 2 years. Thus, as pointed out by Stolwijk-Swüste and colleagues,<sup>57</sup> long-term follow-up studies with unselected study populations and age-matched control individuals are needed to shed further light on this question.

Loss of motor units and a decrease in muscle strength and endurance is not necessarily associated with physical function, physical activity, or social participation. There is no correlation between muscle strength and walking ability in patients with postpolio syndrome.<sup>50,62</sup> The association is non-linear possibly because of compensatory neuromuscular mechanisms.

Daily activity did not decrease during a 3-year follow-up period<sup>63</sup> and participation in walking activities was self-perceived as sufficient for daily life mobility by the patients.<sup>64</sup> Horemans and colleagues<sup>50</sup> and Klein and colleagues<sup>63</sup> found that actual walking in daily life in patients with postpolio syndrome was not only affected by walking capacity but also by social behaviour and personal lifestyle. Willen and colleagues<sup>65</sup> reported that there was a non-linear relation between walking speed and muscle strength. Furthermore, Sorenson and colleagues<sup>66</sup> concluded that there was no association between the amount of decline in motor units and the symptoms of this late muscle deterioration, but minor changes in disability were seen during follow-up.

Increased muscle weakness can lead to reduced balance and increased numbers of falls in patients with previous poliomyelitis.<sup>67</sup> Patients with increased muscle weakness might need to use assistive devices for walking or a wheelchair, and those with weak respiratory muscles might require ventilation.

### Fatigue

Fatigue in patients with postpolio syndrome is multi-dimensional<sup>68</sup> and can be of general or mental character derived from the CNS (caused by early neuronal damage in the brain in the acute poliomyelitis stage, overlapping psychological factors, or both) or muscular from the motor unit.<sup>69-71</sup> Fatigue is probably the most disabling symptom of postpolio syndrome. Muscle weakness during fatigue is caused by slow recovery of the muscle and could reflect both central and peripheral fatigue.<sup>2,72,73</sup> Fatigue in postpolio syndrome has a negative effect on physical and psychosocial functioning but does not impair mental health.<sup>74,75</sup> Health-related quality of life for vitality is to a greater extent caused by physical (eg, decreased physical endurance) than by mental (eg, mental fatigue) parameters.<sup>75</sup> According to Trojan and colleagues,<sup>68</sup> although some risk factors for fatigue (eg,

age and time since the acute poliomyelitis) are non-modifiable, others (eg, stress and physical activity) are modifiable, and hence they are important to consider in the management of these patients.

### Pain

Pain is common in patients with postpolio syndrome; the pain intensity is high<sup>76</sup> and is more often located in parts of the body that were affected by polio than in parts that were not.<sup>77</sup> Many patients with postpolio syndrome report cramping pain in the legs (most often the upper leg musculature) and aching pain in the neck and shoulders.<sup>77</sup> The pain has been reported to be widespread.<sup>78</sup> Pain is most common in women with postpolio syndrome, young patients, or patients who have had a long stable period.<sup>79</sup> Although the pain can have variable origin, it is mostly associated with overload of muscles, tendons, and joints and is related to the amount of physical activity.<sup>77,79-82</sup> 10% of patients with postpolio syndrome have neuropathic pain, caused by secondary disorders such as nerve compression or disc hernia that can be treated.<sup>83</sup> Thorough clinical assessment of patients with postpolio syndrome who have neuropathic pain is therefore needed to exclude concomitant and secondary disorders and to provide adequate pain treatment.

### Hypoventilation

Some patients with polio who had initial weakness of respiratory muscles or other factors that might have decreased lung function (eg, chest deformity or progression of scoliosis) experience new respiratory problems as a consequence of postpolio syndrome.<sup>84</sup> Furthermore, patients with postpolio syndrome are also at risk of nocturnal hypoventilation caused by sleep-disordered breathing (a general term used for different kinds of symptoms related to disorders of breathing during sleep, such as obstructive apnoea, central apnoea, or a mixed dyspnoea). Shortness of breath is the most common complaint, but patients might also present with non-specific symptoms, such as daytime somnolence, morning headache, and fatigue.<sup>84-87</sup> In patients with a history of these symptoms, hypoventilation and sleep-disordered breathing should always be investigated with tests of pulmonary function and polysomnography, respectively. Cardiopulmonary comorbidity should also be considered.

### Other symptoms

Other symptoms and new health problems include cold intolerance, cold sensitivity, muscular twitching, and muscular cramps, as well as concentration problems and swelling of legs and feet.<sup>7,17,88,89</sup> Bulbar muscle weakness can lead to dysphagia and dysphonia.<sup>2,3,7,90,91</sup> Investigation of whether new health problems are caused by postpolio syndrome, are secondary to postpolio syndrome, or are caused by comorbidities is important because some comorbidities require adequate intervention.

### Clinical management

No specific treatment for postpolio syndrome exists. Evaluation of the efficacy of treatment regimens for patients with postpolio syndrome was initiated by the Cochrane Library in 2009. Patients with postpolio syndrome often have a wide range of medical problems and may also have associated problems with participation in society, such as need for technical aids at home and at work.

### Physiotherapy, physical activity, and muscle training

Physical activity forms the basis of management of patients with postpolio syndrome. Most patients with postpolio syndrome benefit from appropriate physical activity and a large proportion benefit specifically from individually chosen muscle training. Lygren and colleagues<sup>78</sup> noted that patients with postpolio syndrome who reported doing regular physical activity had fewer symptoms and a higher level of functioning than those who were not often physically active. No prospective data show that increased physical activity leads to muscle weakness.<sup>6</sup>

Few randomised controlled trials have investigated the effect of muscle training in patients with postpolio syndrome. Because most patients with postpolio syndrome have asymmetrical muscle weakness and the degree of paresis differs over time and between patients, training programmes should be carefully customised and planned by physiotherapists to avoid both overuse and disuse, and the level of physical activity modified to decrease pain.<sup>77,92</sup> Patients should be carefully monitored to identify signs of increasing muscle weakness and muscle pain, and thus to avoid adverse effects, especially overuse of muscles that are clinically unaffected but were found clinically or by use of EMG to be affected by polio infection.<sup>12,16</sup> Overuse-induced weakness has been proposed,<sup>12-15</sup> but there is no evidence that overuse weakness permanently damages muscles affected by poliomyelitis. Rather, the occurrence of overuse-induced weakness could be explained by metabolic demands exceeding the individual muscle capacity or reparable intramuscular damage, similar to those in healthy individuals.<sup>93</sup> In this respect, one must also bear in mind that the energy cost of movement is higher in patients with postpolio syndrome than in control individuals.<sup>94,95</sup>

To save energy, reduction in activity and pacing as well as training in muscle conservation techniques are required; this approach remains the mainstay of treatment of postpolio syndrome.<sup>16,96</sup> Cup and colleagues<sup>97</sup> reviewed studies dealing with exercise therapy in patients with postpolio syndrome and found evidence for effectiveness of strengthening or aerobic exercise to be insufficient.

However, endurance<sup>98,99</sup> and heavy resistance training<sup>100</sup> are effective at increasing muscle strength and endurance in patients with postpolio syndrome. In 1994, the European Neuromuscular Centre workshop<sup>8</sup> on postpolio muscle dysfunction and Grimby and Stålberg<sup>101</sup> recommended guidelines for exercise that are still valid

today. Heavy resistance training was recommended for patients with postpolio syndrome who had near-normal muscle strength and no signs of reinnervation of the motor unit.<sup>8,101</sup> Submaximum endurance training, which increases muscle strength and endurance,<sup>98</sup> was recommended for patients with moderate paresis and signs of reinnervation of the motor unit.<sup>8,101</sup> Patients with severe paresis should avoid muscle training; however, finding a suitable physical activity for cardiovascular conditioning in these patients is important. Aerobic exercise, including bicycle ergometry, treadmill walking, and swimming, are recommended.<sup>2</sup> Aquatic exercise is also beneficial.<sup>102</sup>

### Pharmacological treatment

A few controlled trials of pharmacological treatments have been done in patients with postpolio syndrome. Amantadine and high-dose prednisone were ineffective at reducing muscle weakness and fatigue.<sup>103,104</sup> In one study, no beneficial effect on muscle function was reported after treatment with pyridostigmine.<sup>105</sup> Conversely, another study reported a slight improvement in walking in patients treated with pyridostigmine.<sup>106</sup> In another randomised controlled trial, there was no significant difference in muscle function between patients with postpolio syndrome who were having muscle training and taking coenzyme Q-10 and those receiving placebo.<sup>107</sup> Modafinil has proven ineffective for treatment of fatigue in patients with postpolio syndrome in two randomised controlled trials.<sup>108,109</sup> However, a controlled study on the effect of lamotrigine on pain, fatigue, and quality of life had promising results.<sup>110</sup>

Based on the notion of an inflammatory process in the CNS of patients with postpolio syndrome, intravenous immunoglobulin has been tested. A single course of high-dose intravenous immunoglobulin greatly reduced the concentrations of proinflammatory cytokines in the CSF 2 months after treatment.<sup>27</sup> The idea of a role for these cytokines in postpolio syndrome would be strengthened if a clinical response was also seen, with amelioration of symptoms and signs. In a single patient,<sup>111</sup> in small open studies,<sup>27,112</sup> and in two larger randomised controlled trials,<sup>26,43</sup> variable effects of intravenous immunoglobulin on muscle strength, pain, physical activity, and quality of life have been described. These data encourage further controlled trials to more firmly establish if this treatment regimen should be used. Furthermore, such trials should assess dosing and dosing intervals and ways to predefine responders and non-responders to this treatment.

Symptomatic treatment is of course important in postpolio syndrome. For example, restless legs syndrome is a common complaint in patients with postpolio syndrome and can be successfully treated with dopamine agonists.<sup>113</sup> As pointed out by Trojan and colleagues,<sup>68</sup> the most prominent symptom in postpolio syndrome, fatigue, is multidimensional, and some of the con-

tributing factors can be treated. Other symptomatic pharmacological treatments that should be considered are analgesics and antidepressants.

### Surgery

Joint deformities, arthrosis, and limb-length inequality may require surgery. Increased function can be achieved by arthrodesis, tendon transfers, and muscle transplantation.<sup>114</sup> For other secondary disorders, such as spinal stenosis and disc hernia, surgical treatment can help. However, motor neurons of patients with postpolio syndrome might be more sensitive to effects of anaesthetic drugs and thus patients should be carefully assessed before and monitored both during an operation and postoperatively.<sup>115</sup>

### Orthoses and assistive devices

Orthopaedic braces can restrict unwanted movements—supporting joints and muscles and reducing the impact of bodyweight, particularly in legs and feet. The use of braces should improve mobility, reduce pain, and reduce overuse of the still well functioning parts of the muscles, joints, tendons, and ligaments. Use of lightweight knee–ankle–foot braces can have a beneficial effect (measured as decreased oxygen consumption during walking) and save energy.<sup>116,117</sup>

Patients with postpolio syndrome should be supplied with appropriate orthoses and braces on the basis of individual needs.<sup>118</sup> To further improve energy efficiency, carbon-composite material is preferred.<sup>116,117,119</sup> Besides orthoses, assistive devices to increase functional activity include crutches, manual and electrical wheelchairs, and motorised scooters.<sup>16</sup>

Thorén-Jönsson<sup>54</sup> noted that, despite the need for assistance with mobility, patients with postpolio syndrome associated the use of assistive devices with negative feelings. However, technical developments, including new lightweight and strong materials, have made orthoses and assistive devices more appealing to patients and therefore more useful. Kelley and DiBello<sup>118</sup> have developed a patient classification system that is useful for choosing the right orthotic device.

### Hypoventilation and ventilator support

Some patients with hypoventilation need ventilator assistance. Non-invasive positive pressure ventilation or non-invasive bi-level positive airway pressure ventilation improve quality of life and are preferred by patients, rather than invasive ventilators.<sup>120</sup> Inspiratory muscle training can increase respiratory muscle endurance and wellbeing; however, those patients with chronic respiratory failure are still treated with controlled mechanical ventilation through tracheostomy.<sup>121</sup>

### Lifestyle changes

Lifestyle changes are necessary for many patients with postpolio syndrome. Inactive patients with postpolio

syndrome have a higher risk for late poliomyelitis-related symptoms compared with active people with postpolio syndrome.<sup>122</sup> An active lifestyle should therefore be recommended. However, patients should be carefully assessed to avoid both overexertion and inactivity. Lifestyle modifications can be effective in reducing overuse symptoms.<sup>123</sup> Workload and social interaction in the community<sup>68</sup> should be assessed, and occupational and vocational interventions might be needed.<sup>124</sup> Weight reduction or a programme to stabilise bodyweight may be important.<sup>37</sup> A weight reduction programme, when indicated, can reduce fatigue, improve respiratory symptoms, and increase mobility.

Occupational interventions, weight-control programmes, group therapy (eg, water exercise<sup>125</sup>), and increased use of assistive devices should be considered and managed by the multiprofessional rehabilitation team.<sup>126</sup>

### Future perspectives

Better distinction between postpolio syndrome and poliomyelitis-related secondary disorders by more thorough clinical analyses is important. Further studies are needed to establish if there are clinical markers or risk factors that might predict the development of postpolio syndrome. If identified, measures for preventing postpolio syndrome could be started at an early stage. Further study of subgroups of patients with postpolio syndrome (eg, assessing rate of progression of muscle weakness and different forms of fatigue) and identification of measures to distinguish these subgroups early and thus be able to tailor treatment accordingly are also important.

Pharmacological and rehabilitation interventions seem effective in patients with postpolio syndrome. The study of combinations of these different therapeutic strategies will be important to achieve the best outcomes.

Postpolio syndrome is likely caused by ongoing neurodegeneration, perhaps driven by aberrant chronic

#### Search strategy and selection criteria

References for this Review were identified through searches of The Cochrane Library (1950 to April, 2010), Medline (1950 to April, 2010), Embase (1974 to May, 2009), the Allied and Complementary Medicine Database (1985 to April, 2010), CINAHL (1984 to April, 2010), and Web of Science (1945 to April, 2010) with the search terms “post-poliomyelitis syndrome”, “poliomyelitis survivor”, “late onset poliomyelitis”, “late effect poliomyelitis”, “post-poliomyelitis”, “complications after poliomyelitis”, and “disabilities after poliomyelitis”. The searches were broad and all the terms were truncated and different proximity operators were used. No language restriction was made. Papers were also identified through searches of the authors’ own files. We mostly selected publications from the past 6 years, but we did not exclude important older publications. The reference list was modified according to recommendations from peer reviewers.

inflammation. More effective methods to halt the progression of neurological deficits in postpolio syndrome will probably require a deeper understanding of the pathophysiology of these processes. We envisage efforts to characterise biomarkers for postpolio syndrome, such as certain cytokines or other biochemical markers associated with clinical progression. Such markers would be of importance for monitoring pharmacological and rehabilitation interventions. Immunological, virological, and genetic approaches will be needed to increase the knowledge of the pathophysiology of postpolio syndrome. With this information, hopefully tailor-made and more specific and effective interventions might be possible, particularly in the early stages of postpolio syndrome.

#### Contributors

HG and KB did the literature search and TO edited the Review. All authors wrote the Review.

#### Conflicts of interest

HG has received fees as a senior consultant for Pharmalink. TO has received fees for consultancy from Sanofi-Aventis, Merck Serono, and Biogen Idec. KB has received consultancy fees from Pharmalink.

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