Poliomyelitis

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Summary

1996 is polio awareness year. This paper reviews the clinical syndrome of acute paralytic poliomyelitis and its sequelae. We discuss epidemiological studies of the syndrome of late functional deterioration many years after the acute infection and the current hypotheses of the pathophysiology of such disorders. Recent evidence has suggested that potentially treatable factors may be implicated in the majority of such patients and it is therefore important to exclude such disorders before attributing late functional deterioration to progressive postpolio muscular atrophy.

Keywords: poliomyelitis, post-polio syndrome

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In 1988 the World Health Organisation declared its commitment to the global eradication of paralytic poliomyelitis by the year 2000.*[1]* This has been achieved in most countries of the Western Hemisphere using strategies relying on (a) mass vaccination campaigns using live attenuated oral polio vaccine in all children under the age of five years, (b) enhanced surveillance, and (c) targeting immunisation to areas and populations where poliovirus transmission is likely to persist.*[2]* However, wild-type poliomyelitis continues to occur in regions with high rates of endemic poliomyelitis and, rarely, in outbreaks in areas believed to be free of the disease.*[3]*

There has recently been a great deal of interest in the syndrome of late functional deterioration occurring many years following acute paralytic poliomyelitis.*[4]* Following the large epidemics of the 1940s and 1950s many patients have presented with new neuromuscular symptoms and there is an incomplete understanding of the pathogenesis of such symptoms.

In this paper, we review the clinical features and pathology of the acute illness and make an appraisal of the current understanding of the pathogenesis of the so-called 'post-polio syndrome'.

Acute infection

Poliomyelitis is caused by an enterovirus of high infectivity whose main reservoir of infection lies in the human gastrointestinal tract. There are three subtypes but, prior to vaccination, type 1 accounted for 85% of cases of paralytic illnesses.*[5]* The route of infection is oral - oral and faecal - oral. Viruses multiply in the pharynx and intestine during the one-to-three-week incubation period before blood-borne dissemination occurs. The virus continues to be excreted in the saliva for two or three days, and in the faeces for a further two or three weeks. Cases are most infectious seven to 10 days before and after the onset of symptoms. The infection rate in households with young childen can reach 100%. It is thought that 95% of all infections are asymptomatic or selflimiting 'flu-like' illnesses.*[6]*

Prior to vaccination, the disease had a worldwide distribution. Epidemics occurred during summer months and were more frequent in the temperate climates of the Northern Hemisphere, while the incidence was greater in areas of poor sanitation. Following the introduction of mass vaccination programmes in the late 1950s and early 1960s the incidence of paralytic poliomyelitis has been dramatically reduced in countries with these programmes. In such countries, approximately 50% of cases are caused by live vaccine virus in adult contacts of vaccinated infants, and 25% of illnesses occur in the vaccine recipient.*[7-9]* The remaining infections are thought to be due to wild virus infection in nonimmunised people. Polio-like illnesses are associated with infection by other enteroviruses, particularly Coxsackie A and B and echoviruses,*[10]* and epidemics of paralytic illness due to infection with EV 70 and 71, which causes acute haemorrhagic conjunctivitis, have recently been reported.*[11,12]*

In England and Wales there were 21 cases of paralytic poliomyelitis between 1985-1991.*[13]* Five of these were imported and the source of infection unknown, and 13 cases were vaccine associated, of whom nine occurred in the recipient. Unsuspected immune deficiency was found in two of the infant cases. The remaining three cases occurred in previously healthy unimmunised adolescent or adult contacts of infants who had received their first immunisation.

NON-PARALYTIC OR PRE-PARALYTIC POLIOMYELITIS

Following a prodromal illness, patients develop a high fever with pharyngitis, myalgia, anorexia, nausea and vomiting, and headache with neck stiffness due to meningitis. In the nonparalytic illness the symptoms tend to subside within one or two weeks.

PARALYTIC POLIOMYELITIS

It remains unclear which factors favour the development of paralytic disease but there is some evidence that physical activity and intramuscular injections during the prodrome may be important exacerbating influences.*[14]* Following the meningitic phase, most patients develop a spinal type of poliomyelitis, in which severe muscle pain arises, often with muscle spasms, then weakness and fasciculation develops. Weakness tends to be asymmetrical, the lower limbs being more often affected than the upper limbs, it

tends to become maximal within 48 hours, particularly in children. A biphasic form may arise in which further weakness occurs following a short period of stability, but no further weakness occurs once the fever has settled. Muscle tone is flaccid, the reflexes are initially brisk, then become absent. Paraesthesiae are common, but there is usually no objective sensory loss.

A purely bulbar form may occur, without limb weakness, particularly in children, and is said to be more common in those whose tonsils and adenoids have been removed.*[15]* Adults tend to have spinal as well as bulbar involvement. Although any cranial nerve nucleus may be involved, the most frequently affected lie in the medulla leading to dysphagia, dysphonia and respiratory failure.*[16]* Vasomotor disturbances such as hypertension, hypotension and circulatory collapse contribute to the high mortality of this form of the disease. Other forms of autonomic dysfunction may also be prominent, with disturbances of micturition and gastrointestinal paresis.

The encephalitic form is rare and manifests as agitation, confusion, stupor and coma. Autonomic dysfunction is common and has a high mortality.

In a series of 201 patients seen over a 25-year period from 1935,*[17]* spinal paralysis occurred in 60%, of whom it was considered mild in 33%, moderately severe in 40% and severe in 27%; 20% had bulbar paralysis, 22% had required ventilation and the mortality was 11.4%. Paralysis remains static for several days or weeks before a slow recovery occurs over several months or years.*[18]*

DIAGNOSTIC TESTS

The virus may be isolated from the nasopharynx for five days and from the stools for up to five weeks after the onset of symptoms . It is rarely isolated from the cerebrospinal fluid (CSF) or serum, in contrast to the paralytic illnesses caused by other enteroviruses*[19,20]* which can be identified with polymerase chain reactions. Following isolation, the virus is serotyped using strain-specific antisera and allowing differentiation of wild-type from vaccine-induced disease. Following infection with type 1 poliovirus there is an acute rise in serum IgM titre with IgG antibody developing over about three months. The CSF shows increased protein content, pleocytosis (neutrophils in the first few days then lymphocytes) with a normal sugar. The earliest electromyographic finding is a reduction in the recruitment pattern and a diminished interference pattern. Following paralysis the muscle is electrically silent at rest. Fibrillations develop in two to four weeks and persist indefinitely, fasciculations may also be seen. Motor unit action potentials are reduced, but return during recovery, then become abnormally large in amplitude with increased duration and polyphasia, owing to reinnervation. The motor conduction velocities remain normal.*[21,22]*

The diagnosis of acute paralytic poliomyelitis is usually clear in the presence of an asymmetric purely motor flaccid paralysis with an aseptic meningitis; the differential diagnosis principally includes other forms of neuromuscular causes of acute paralysis such as Guillain-Barre syndrome, in which the CSF is characteristically acellular and nerve conduction velocities are prolonged, and that due to acute intermittent porphyria, HIV, diphtheria and *Borrelia bergdorferi* (Lyme disease) infections, and disorders at the neuromuscular junction such as triorthocresylphosphate poisoning and botulism.

PATHOLOGY OF ACUTE PARALYTIC POLIOIMYELITIS

The poliovirus rapidly becomes widely disseminated throughout the central nervous system; early changes are of neuronal chromatolysis, particularly affecting the cytoplasmic Nissl substance, and a perivascular inflammatory cell infiltrate. Disintegration of the nucleus occurs, followed by necrosis and lysis of the

whole cell. The severity of the paralysis correlates with the proportion of the neurons destroyed.*[23]* During the acute infection only about 5% of neurons in an affected area remain intact and there is also extensive involvement in clinically unaffected areas. Approximately 50% of involved neurons are destroyed. Gliosis develops when the inflammatory infiltrate has subsided, but most surviving neurons show full recovery.

The most common sites for the pathological change to be seen are the anterior horn cells of the cord and neurons in the intermediate, intermediolateral and posterior horns, and occasionally the dorsal root ganglia. The cerebellar vermis and the brainstem nuclei, particularly the nucleus ambiguous, V, VII, XII and vestibular nuclei and the reticular formation in the medulla, pens and midbrain may all be affected. *[23]* In the cerebral cortex the precentral gyrus is frequently affected as well as the hypothalamus, thalamus and globus pallidus.

TREATMENT OF THE ACUTE ATTACK

All patients should be put to bed in isolation. Careful observation should be made of bulbar function, vital capacity and cardiovascular responses in order to anticipate the development of respiratory and circulatory complications. Pain relief, splinting of joints and frequent passive movements prevent contractures and joint ankylosis.

Acute respiratory failure is due to medullary involvement leading to impaired central rhythm generation or to respiratory muscle weakness or to a combination of both. During the large epidemics of the 1940s and 50s, most patients received negative pressure ventilation in an iron lung. This is an efficient form of ventilation particularly suited to paralysed and deformed patients which allows concurrent physiotherapy and postural drainage. Severe bulbar weakness necessitates a tracheotomy to protect the airway and under these circumstances intermittent positive pressure ventilation is preferable during the acute illness.

PREVENTION

Salk trivalent inactivated polio vaccine was introduced in 1956 for routine immunisation. This vaccine is administered by injection and stimulates serum IgM, IgG and IgA but not secretory IgA, immunity being induced by antibody transuding into the oropharynx. It is highly effective and remains indicated in pregnant, immunosuppressed and unvaccinated individuals over the age of 50 years. Sabin trivalent oral live attenuated polio vaccine replaced the Salk vaccine in 1962; this is composed of live attenuated strains of polioviruses I, II and III grown in cell culture. The advantages over the Salk vaccine is that it can be administered orally and causes an active attenuated infection of the oropharynx and intestinal endothelium leading to local secretary IgA in addition to serum antibody production. Furthermore, the attenuated virus is excreted in the faeces producing herd immunity. Individuals born before 1958 may not have been immunised and no opportunity should be missed to immunise them in adult life. Unimmunised contacts of recently immunised infants are at particular risk of infection when changing nappies and must be vaccinated. Oral polio vaccine is recommended for infants from two months of age. The primary course consists of three separate doses with intervals of one month in between doses.

Global eradication depends on achieving high vaccination coverage in all regions. This has been attempted by rigorous surveillance with better case definition and the use of mass campaigns of immunisation in remote areas together with carefully planned "mopping up" operations targeting areas with high infection rates.*[2,3]* There are problems with this plan; it has proved difficult to provide adequate heat-stable Sabin vaccine and it is also impossible to ensure adequate seroconversion in tropical populations leading to point outbreaks. The political and financial cost of this undertaking remain

enormous.

Late post-polio deterioration

It is clear that, after a period of prolonged stability, many patients with previous paralytic poliomyelitis may develop late functional deterioration manifest as impairment of mobility, upper limb function, respiratory capacity and activities of daily living. The first published report is attributed to Raymond who presented a case to Charcot in 1875*[24]* in which a man developed left-sided weakness and muscle wasting following a febrile illness at the age of six months, and had presented at the age of 17 years with weakness, fasciculation and wasting of the right arm and leg. Much has also been written about the illness of Franklin D Roosevelt who contracted polio at the age of 39 and had functional deterioration later in life.*[25]* In 1962, Zilkha reported from the National Hospital eleven further cases in which patients studied retrospectively showed new weakness in muscle groups felt not to have been involved clinically in the acute disease but who presented 17-43 years later with new weakness and fasciculation.*[26]* He considered that previous poliomyelitis may predispose patients to the subsequent development of motor neuron disease.

Investigation of patients with late functional deterioration following poliomyelitis
blood investigation: ESR for chronic infection or occult malignancy, haemoglobin for anaemia, renal and liver profiles, bone profile for metabolic bone disease, fasting glucose, creatine kinase for polymyositis, thyroid function tests
X-ray: joints and spine for degenerative change and deformity
MRI: spine for myelopathy or spinal stenosis
chest X-ray and pulmonary function tests: evidence of chronic lung disease and scoliosis
psychiatric assessment: depressive illness
EMG/NCV: to assess the residual effects of the original infection and its extent and to identify any superimposed neuromuscular disorder, such as entrapment neuropathy, radiculopathy, peripheral neuroparhy, neuromuscular junction disease or muscle disease

This late deterioration has been referred to as the 'post-polio syndrome' by several authors, although the definition of this disorder varies. Bradley*[27]* included all causes of progressive musculoskeletal deformities, nerve entrapments and pain syndromes due to the original muscle weakness. Dalakas*[28]* and Halstead*[29]* included complaints such as fatigue, muscle and joint pain, reduced exercise tolerance, impairment of acrivities of daily living, limb atrophy, cramps and fatigue and specifically excluded musculoskeletal symptoms due to back injuries, radiculopathy, compression neuropathies and other medical, neurological, orthopaedic or psychiatric illnesses. All these definitions of post-polio syndrome also include the condition of progressive post-polio muscular atrophy; this diagnosis can be made when there is a new history of decreased muscle strength, weakness and/or atrophy in an asymmetrical distribution compatible with previous polio, and electrophysiological features of acute denervation superimposed on chronic denervation-reinnervation in the absence of another neuromuscular cause.*[27]* Dalakas and his colleagues did not include the electromyographic criteria but considered progressive post-polio muscular atrophy to be present when there is evidence of new muscle atrophy and weakness either in clinically affected or unaffected muscles, occasional pain and fasciculations in newly symptomatic or even asymptomatic muscles, and new bulbar, respiratory or sleep difficulties occurring in patients with

residual bulbar and respiratory muscle weakness. These criteria may be considered somewhat inconsistent as they include musculoskeletal abnormalities which can be directly related to the post-polio disability yet they apparently exclude entrapment neuropathy, radiculopathy and orthopaedic problems which may also be attributed to the original illness.

Although original reports suggested an association between polio and motor neuron disease, this has not been confirmed by subsequent observation . Indeed Armon *et al*[30] noted the relative paucity of classical amyotrophic lateral sclerosis developing in survivors of paralytic poliomyelitis, and Swingler *et al*[31] were unable to show any geographical association between past mortality from poliomyelitis and present morbidity and mortality from motor neuron disease in a Scottish population.

Although late functional deterioration may be severe[27,32] the progressive post-polio muscular atrophy syndrome appears to be a relatively mild disorder in which the weakness often cannot be appreciated on a year to year basis.[29] In an uncontrolled series, Dalakas *et al* reported 27 patients with variable but severe weakness in whom clinical assessment was based on annual examination of 20 muscles using Medical Research Council grading .[33] The authors showed a 1% per year decline over a mean follow-up period of 8.2 years. In this series postpolio syndrome was unrelated to any other neurological or medical disorder and, surprisingly, no patients were reported to have progressive scoliosis although in our patients this has been an extremely common finding in those who develop acute poliomyelitis before the growth spurt.[32]

It is possible that post-polio syndrome may be the clinical manifestation of a continuous and widespread process of denervation and reinnervation occurring in all muscles clinically and subclinically affected by the original poliomyelitis. This is suggested by electrophysiological evidence of active denervation including spontaneous activity and increased fibre density with jitter and blocking on single fibre studies in both affected and unaffected muscle groups in patients with and without post-polio syndrome.[34-36] Furthermore, muscle biopsy studies have shown features of ongoing denervation including small angulated fibres, group atrophy and fibre type grouping in both stable patients and those with late onset deterioration.[35,37,38]

AETIOLOGY

A number of possible mechanisms have been suggested to account for postpolio syndrome.[28,39] Late post-polio deterioration may represent the normal neuronal loss of ageing reflected in pools of anterior horn cells critically reduced during previous polio infection; however, neuronal loss is rarely seen before the age of 60 years,[40] and the development of post-polio syndrome depends on the severity of the acute illness rather than the age of the patient.[28]

Immunological mechanisms are suggested by the presence of mild inflammatory changes in muscle biopsy[35,37,38] and the mild active pathological changes seen in the spinal cord.[41] The presence of persistent or recurrent viral infection was suggested by the finding of an intrathecal IgM antibody response to poliovirus in many patients with post-polio syndrome.[42] Subsequent studies of CSF using polymerase chain reaction and fresh *post-mortem* tissue have shown that enterovirus RNA may persist in the central nervous system of patients with previous poliomyelitis but the biological and clinical significance of these findings remains uncertain[43] and this has not been seen in other Studies.[44,45]

Finally, it is possible that post-polio syndrome represents a process of attrition and premature neuronal exhaustion. During the acute illness there is a large loss of motor neurons; during recovery the terminal axons of surviving motor neurons sprout in an attempt to re-innervate muscle fibres orphaned by the death

of their parent motor neurons giving rise to the development of large motor units. However, these new reinnervated motor units are unstable with continuing preterminal sprouting and ongoing denervation and re-innervation. This continuous process of denervation and re-innervation stresses neuronal cell bodies left with diminished reserves and reduced ability to maintain the metabolic demands on all their sprouts. There may then be a gradual loss of terminal sprouts to single fibres, ultimately leading to the development of atrophy in adjacent fibres.

Whilst the clinical and electrophysiological characteristics of the post-polio syndrome have been defined, it remains unclear what proportion of late functional deterioration can be attributed to it or to progressive post-polio muscular atrophy and how many patients have clearly defined medical or surgical causes. Published series of patients with post-polio syndrome give little impression of the relative frequency of clear underlying causes for functional deterioration in patients with previous poliomyelitis.

In a retrospective review of 29 patients admitted between 1965 and 1990 with late deterioration, six of these patients were considered to have progressive musculoskeletal deformities resulting from the original weakness and 23 to have post-polio syndrome, although this included three patients with signs of upper motor neuron lesions.*[46]*

Howard *et al[32]* reported a series of 209 consecutive patients of whom 163 (78%) developed late functional deterioration due to respiratory factors in 99 cases, neurological signs in 20 cases and orthopaedic problems in 17 cases; 31 patients deteriorated due to a combination of factors. Scoliosis developed in 94 patients (45%) and was invariable if paralytic poliomyelitis occurred before the growth spurt. Functional deterioration was associated with progressive scoliosis in at least 18 patients; 34 patients (16%) had worsening limb function associated with difficulty using callipers, cervical spondylosis, osteoarthritis, osteoporosis, back pain and contractures. Other conditions were also relatively frequent in this population of severely disabled patients and the following factors contributed to the progressive functional deterioration: chronic urinary symptoms secondary to calculi, severe trophic changes of the legs, hypertension, depression, diabetes mellitus, peptic ulceration, thyroid disorders and pregnancy.

Windebank *et al* from the Mayo Clinic published a series in which a group of 50 patients representative of a possible group of 247 patients who had had paralytic polio in Olmsted county, Minnesota, had been carefully reassessed.*[47]* Although 64% reported new symptoms, only 18% were found to have undergone any form of functional deterioration. Crucially, since the Mayo Clinic Neurology department has for many years used a standardised scoring system for all neurological examinations, it was found that even though patients reported new or worsening weakness, in all but four patients, this was not substantiated when the follow-up scores were compared with the old ones. In the four patients in whom new or worsening weakness was substantiated, reasonable evidence for the development of a superimposed neurological disorder causing the change had been found (eg, diabetic neuropathy).

Studies from our own department have also failed to identify a single case of progressive post-polio muscular atrophy; a recently reported series of 158 patients who had presented with symptoms of late functional deterioration showed that orthopaedic and neurological complications such as osteoarthritis, cervical spondylosis and entrapment neuropathies accounted for the deterioration in 90% of cases.*[48]*

It is of particular interest that the Mayo Clinic series has been prospectively followed up;*[49]* the frequency of symptoms of late deterioration did not change over the five-year period, and the neurological examination findings and test of manual dexterity were unaltered. A mean timed 100-ft walk actually improved. The electromyographic studies were also unchanged.

CAUSES AND MANAGEMENT OF LATE FUNCTIONAI. DETERIORATION

Orthopaedic complications

Orthopaedic complications are extremely common and reflect the prolonged abnormal stresses applied to joints due to muscle weakness. Abnormalities include fixed flexion deformities, hyperextension or lateral instability of the knee *(figure 1)* or hip, and progressive instability of joints, fractures, osteoporosis, osteoarthrosis and scoliosis *(figure 2)*. Cervical spondylosis is manifested by neck pain and variable radicular sensory symptoms and cord compression occurs in some patients *(figure 3)*. Many aspects of the management of these patients involve detailed and specialised orthopaedic assessment. A range of simple supports to knee, ankle and cervical spine, or correction of worn and damaged aids may provide considerable functional improvement. This includes the provision of new callipers, braces, foot orthoses, knee and pelvic supports, shoe raises, collar, harness and seating.

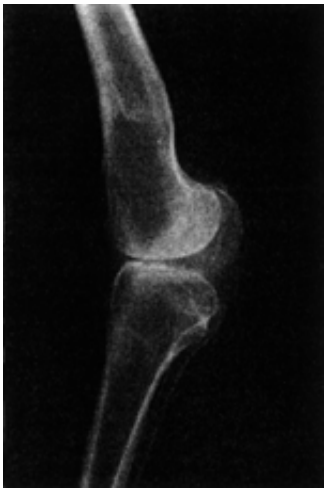

Figure 1

X-ray of the right knee in a patient with genu recurvatum

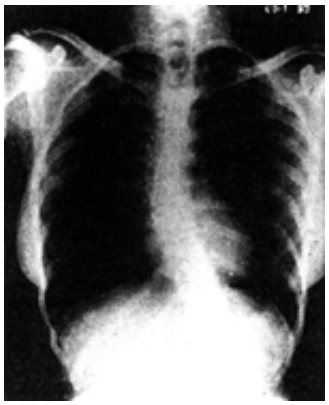

Figure 2

Chest X-ray showing severe dorsal scoliosis

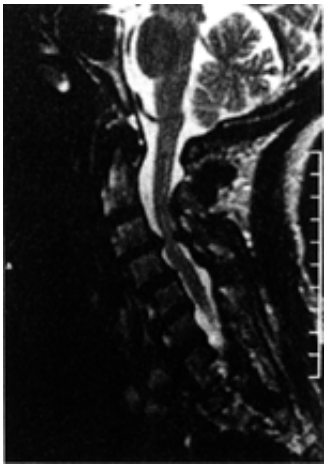

Figure 3

MRI scan of cervical spine showing cervical cord compression by osteophytes and prolapsed intervertebral discs

Cervical decompression is usually indicated in the presence of severe established radiculopathy or myelopathy. If progressive scoliosis is contributing to respiratory insufficiency then spinal surgery may be undertaken. Hip and knee deformities are corrected with physiotherapy, hydrotherapy, night splints or foam supports and instabilities are treated with the provision of more appropriate orthoses. With severe bilateral genu recurvatum causing posterior knee pain, if orthotic support fails, bone block procedures using the patella have proved effective.*[50]* Obesity frequently contributes to orthopaedic deterioration.

Neurological deterioration

Skeletal deformity due to previous poliomyelitis contributes to the development of multiple peripheral nerve entrapments leading to functional deterioration. Other neurological disturbances coexisting with previous polio have included motor neuron disease,*[30]* multiple sclerosis,*[51]* syringomyelia, epilepsy and meningioma. There is no evidence to suggest these associations are anything but coincidental.

Respiratory insufficiency

Respiratory insufficiency is associated with progressive nocturnal hypoventilation due to chest wall

deformity, progressive scoliosis or other factors stressing critically compromised ventilation. These include respiratory tract infections, obstructive airways disease, tracheostomy complications, obesity and pregnancy.*[32,52,53]* The strategies and methods of artificial ventilation used in poliomyelitis are long established but require special adaption in the presence of scoliosis. The indications for the use of positive and negative ventilation have been described in detail previously.*[54]*

Other contributory factors

Other general medical factors contributing to late functional deterioration include diabetes, hypertension and depression.

Conclusions

In several large series late functional deterioration has been associated with clear medical or surgical factors. Using conventional definitions these patients could not be considered to have post-polio syndrome. Rather the severe physical stresses of post-polio disability leads to the development of progressive orthopaedic, respiratory, orthopaedic and general medical abnormalities, often exacerbated by intercurrent events. These abnormalities may often present with atypical clincal features because of the extent of underlying atrophy and weakness. Many of these abnormalities are potentially treatable and it is therefore necessary to urge caution before attributing functional deterioration to the post-polio syndrome or progressive post-polio muscular atrophy.

REFERENCES

1. World Health Organisation (WHO) Global eradication of poliomyelitis by the year 2000. *WHO Weekly Epidemiol Rec* 1988; **63:** 161-2.
2. Hall AJ. Polio eradication as 2000 approaches. *BMJ* 1992; **305:** 69-70. [PubMed Abstract]
3. Hull HF, Ward NA, Hull BP, Milsten JB, de Quadros C. Paralytic poliomyelitis: seasoned strategies, disappearing disease. *Lancet* 1994; **343:** 1331-7. [PubMed Abstract]
4. Dalakas MC, Bartfield H, Kurland LT, eds. The post-polio syndrome: advances in the pathogenesis and treatment. *Ann NY Acad Sci* 1995; **753.**
5. Sabin AB. Poliomyelitis. In: Horsfall FC, Tamm I, eds.*Viral and rickettsial infections of man.* 5th edn. Philadelphia: JB Lippincott, 1980; p 1348.
6. Jubelt B, Lipton HL. Enterovirus infections. In: Vinken PJ, Bruyn GW, Klawens HL, McKendall RR, eds. *Handbook of clincal neurology*, revised series, vol 56: Viral disease. Amsterdam: Elsevier Science Publishers BV, 1989; pp 314-6
7. Nkowane BM, Wassilaki SGF, Orenski WA, *et al*. Vaccine-associated paralytic poliomyelitis; United States 1973 through 1984. JAMA 1987; **217:** 1335-40. [PubMed Abstract]
8. Arlazoroff A, Bleicher Z, Klein C, et al. Vaccine associated contact paralytic poliomyelitis with atypical neurological presentation. *Acta Neurol Scand* 1987; **76:** 210-14. [PubMed Abstract]
9. Querfurth H, Swanson PD. Vaccine-associated paralytic poliomyelitis: regional case series and review. *Arch Neurol* 1990; **47:** 541-4. [PubMed Abstract]
10. Gear JH. Nonpolio causes of polio-like paralytic syndromes. *Rev Infect Dis* 1984; **6:** S379-84. [PubMed Abstract]
11. Katiyar BC, Misra S, Singh RB, *er al*. Adult polio-like syndromes following enterovirus 70 conjunctivitis. *Acra Neurol Scand* 1983; **67:** 263-74. [PubMed Abstract]
12. Chumakov M, Vorashilova M, Shindarov L, *et al*. Enterovirus 71 isolated from cases of epidemic poliomyelitis-like disease in Bulgaria. *Arch Virol* 1979; **60:** 329-40. [PubMed Abstract]

13. Joce R, Wood D, Brown D, Begg N. Paralytic poliomyelitis in England and Wales 1985-1991. *BMJ* 1992; **305:** 79-82. [PubMed Abstract]
14. Russell WR. Paralytic poliomyelitis - the early symptoms and the effect of physical activity on the course of the disease. *BMJ* 1949; **i:** 465 - 71.
15. Anderson GW, Rondeau SL. Absence of tonsils as a factor in the development of bulbar poliomyelitis. *JAMA* 1954; **155:** 1123-30.
16. Plum F, Swanson AG. Central neurogenic hyperventilation in man. *Arch Neurol Psychiatry* 1959; **81:** 531-49.
17. Codd MB, Mulder DW, Kurland LT, Beard CM, O'Fallon WM. Poliomyelitis in Rochester, Minnesota 1935-1955: epidemiology and longterm sequelae - a preliminary report. In: Halstead LS, Wiechers DO, eds. *Late effects of poliomyelitis.* Miami: Symposium Foundation, 1985; pp 121-34.
18. Green WT. The management of poliomyelitis: the convalescent stage. In: *Poliomyelitis: papers and discussions presented at the first international poliomyelitis conference.* Philadelphia: Lippincott, 1949;pp 165-85.
19. Muir P, Nicholson F, Jhetam M, Neogi S, Banatvala JE. Rapid diagnosis of enterovirus infection by magnetic bead extraction and polymerase chain reaction detection of enterovirus RNA in clinical specimens. *J Clin Microbiol* 1993; **31:** 31-8. [PubMed Abstract]
20. Zoll GJ, Melchen WJG, Kopecka H, et al. General primer mediated PCR for the detection of enteroviruses; application for diagnostic routine and persistent infections. *J Clin Microbiol* 1992; **30:** 160-5. [PubMed Abstract]
21. Johnson EW, Guyton JD, Olsen KJ. Motor nerve conduction velocity studies in poliomyelitis. *Arch Phys Med Rehabil* 1960; **5:** 185-90.
22. So YT, Olney RK. AAEM case report no. 23: acute paralytic poliomyelitis. *Muscle Nerve* 1991; **14:** 1159-64. [PubMed Abstract]
23. Bodian D. Histopathologic basis of clinical findings in poliomyelitis. *Am J Med* 1949; **6:** 563-78.
24. Raymond M. Paralysie essentialle de l'enfance atrophie musculaire consecutive. *Gaz Med Paris* 1875; 226.
25. Gallagher HG. *FDR's splendid deception.* New York: Dodd Mead, 1985.
26. Zilkha KJ. Discussion on motor neurone disease. *Proc R Soc Med* 1962; **55:** 1028-9.
27. Bradley WG. Recent views on amyotrophic lateral sclerosis with emphasis on electrophysiological studies. *Muscle Nerve* 1987; **10:** 490-502. [PubMed Abstract]
28. Dalakas MC, Hallett M. The post polio syndrome. In: Plum F, ed. *Advances in contemporary neurology* Philadelphia: FA Davis, 1988: pp 61-81.
29. Halstead LS, Wiechers DO, eds. *Research and clinical aspects of the late effects of poliomyelitis* White Plains: March of Dimes, 1987.
30. Armon C , Daube JR, Windebank AJ, Kurland LT. How frequently does classic amyotrophic lateral sclerosis develop in survivors of poliomyelitis? *Neurology* 1990; **40:** 172-4. [PubMed Abstract]
31. Swingler RJ, Frazer H, Warlow CP. Motor neurone disease and polio in Scotland. *J Neurol Neurosurg Psychiatry* 1992; **55:** 1116-20. [PubMed Abstract]
32. Howard RS, Wiles CM, Spencer GT. The late sequelae of poliomyelitis. *Q J Med* 1988; **251:** 219-32. [PubMed Abstract]
33. Dalakas MC, Elder G, Hallett M, *et al*. A long term follow-up study of patients with post polio neuromuscular symptoms. *N Engl J Med* 1986; **314:** 959-63. [PubMed Abstract]
34. Weichers DO, Hubbell SL. Late changes in the motor unit after acute poliomyelitis. *Muscle Nerve* 1981; **4:** 524-8. [PubMed Abstract]
35. Cashman NA, Maselli R,Wollmann RL, Roos R, Simian R, Antel JP. Late denervation in patients with antecedent paralytic poliomyelitis. *N Engl J Med* 1987; **317:** 7-12. [PubMed Abstract]
36. Ravits J, Hallett M, Baker M, Nilsson J, Dalakas MC. Clinical and electromyographic studies of

post polio progressive muscular atrophy. *Muscle Nerve* 1990; **13:** 667-74. [PubMed Abstract]
37. Drachmann DB, Murphy SR, Nigan NP, Hill JR. Myopathic changes in chronically denervated muscle. *Arch Neurol* 1967; **16:** 14-24. [PubMed Abstract]
38. Dalakas MC. Morphologic changes in the muscle of patients with post polio neuromuscular symptoms. *Neurology* 1988; **38:** 99-104. [PubMed Abstract]
39. Jubelt B, Cashman NA. Neurological manifestations of the postpolio syndrome. *CRC Crit Rev Neurobiol* 1987; **3:** 207-11. [PubMed Abstract]
40. Tomlinson BE, Irving D. The number of limb motor neurones in the human lumbosacral cord throughout life. *J Neurol Sci* 1977;**34:** 217-9. [PubMed Abstract]
41. Pezeshkpour GH, Dalakas MC. Longterm changes in the spinal cord of patients with old poliomyelitis: evidence of active disease. *Arch Neurol* 1988; **45:** 505-8. [PubMed Abstract]
42. Sharief MK, Hentges R, Ciardi M. Intrathecal immune response in patients with the postpolio syndrome. *N Engl J Med* 1991; **325:** 749-55. [PubMed Abstract]
43. Muir P, Nicholson F, Ajetunmobi J, *et al*. Detection of enterovirus RNA in the CNS of patients with previous paralytic poliomyelitis (abstract). *J Neurol Neurosurg Psychiatry* 1995; **59:** 216.
44. Melchers W, de Visser M, Jongen P, *et al*. The postpolio syndrome: no evidence for poliovirus persistence. *Ann Neurol* 1992; **32:** 728-32. [PubMed Abstract]
45. Roivainen M, Kinnunen K, Hovi T. 21 patients with strictly defined post polio syndrome - no poliovirus-specific IgM in patients in the cerebrospinal fluid. *Ann Neurol* 1994; **36:** 115-6. [PubMed Abstract]
46. Miranda-Pfeilsticker B, Figarella-Branger D, Pellissier JF, Serratrice G. Le syndrome postpoliomyélitique: 29 cas. *Rev Neurol* 1992; **148:** 355-61. [PubMed Abstract]
47. Windebank AJ, Litchey WJ, Daub JR, Kurland LT, Codd MB, Iverson R. Late effects of paralytic poliomyelitis in Olmsted County Minnesota. *Neurology* 1991; **41:** 501-7. [PubMed Abstract]
48. Kidd D, Howard RS, Chroni E, Heatley FW, Williams AJ, Spencer GT. A study of late functional deterioration in previous paralytic poliomyelitis (abstract). *J Neurol Neurosurg Psychiatry* 1995; **59:** 203.
49. Windebank AJ. Differential diagnosis and prognosis. In: Halstead LS, Grimsby G, eds. *Postpolio syndrome*, Philadelphia: Hanley & Beifus Inc, 1995; pp 69-88.
50. Men Hong-Xue, Bian Chan-Hua, Yang Chan-Dou, Zhang Zen-Long, Wu Chi-Chang, Pang Be-You. Surgical treatment of the flail knee after poliomyelitis. *J Bone Joint Surg* 1991; **73:** 195-9.
51. Chroni E, Howard RS, Panayiotopoulos CP, Spencer GT. Multiple sclerosis presenting as late functional deterioration after poliomyelitis. *Postgrad Med J* 1995; **71:** 52-4. [PubMed Abstract]
52. Nichols PJR, Lane DJ, Hamilton EA, Hazleman BL. Late onset respiratory failure after poliomyelitis. *Lancet* 1972; **ii:** 1320. [PubMed Abstract]
53. Lane DJ, Hazleman B, Nichols PJR. Late onset respiratory failure in patients with previous poliomyelitis. *Q J Med* 1974; **172:** 551-68. [PubMed Abstract]
54. Howard RS, Spencer GT. Neurogenic respiratory failure. In: Greenwood R, Barnes MP, McMillan TM, Ward CD, eds. *Neurological rehabilitation*. Edinburgh: Churchill Livingstone, 1993; pp 299-310.

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