Forgotten and neglected: The late effects of poliomyelitis

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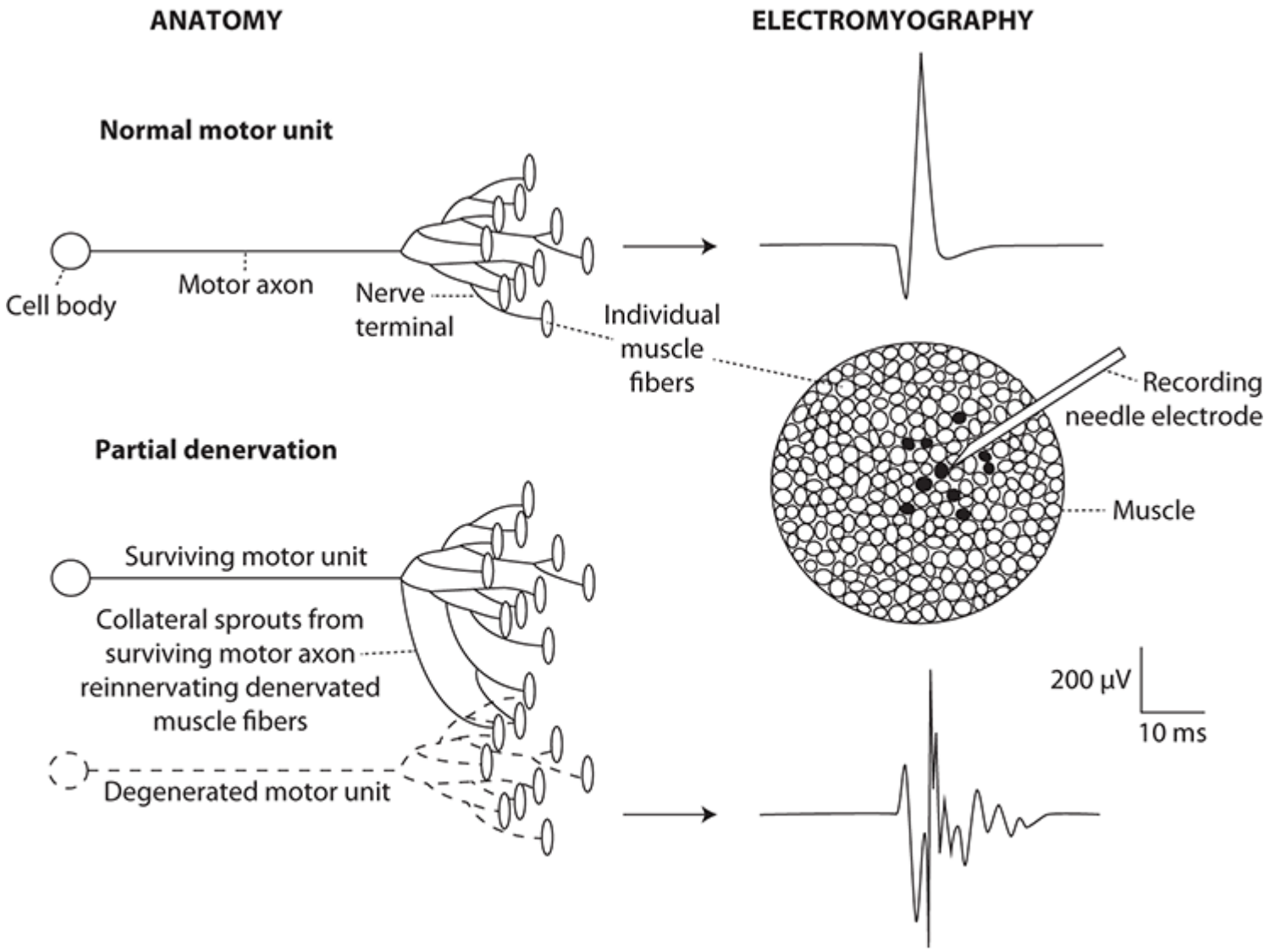
Poliomyelitis

- The polio virus is an enterovirus with extremely high infectivity:
  - During epidemics 85%-100% of individuals in an affected community are infected [cf: 10%-20% with influenza virus].
  - Most infections are asymptomatic (~70%).
  - Many cause mild febrile illness with pharyngitis and gastroenteritis (~25%).
  - Some develop aseptic meningitis without paralysis (~2-4%)
  - Only ~0.5% of exposed individuals develop clinically evident paralytic polio.
- Estimated to have been and average of ~200 cases/year in NZ between 1910 and 1960 but it occurred in epidemics so in some year it was more frequent.
- There may be as many as 12000 polio survivors living in NZ presently.
- Almost certainly much more frequent but undiagnosed.

Poliomyelitis

- Invasion of motor neurons (anterior horn and motor brainstem cells) usually results in irreversible degeneration.
- Complete or partial recovery occurs by way of collateral axonal sprouting of surviving motor neurons.
- Some sub-lethally affected motor neurons could possibly recover.
- Subtle damage to long tracts (motor and sensory) could occur, probably as an “innocent bystander” effect.

- Full or effective motor function may be restored by as few as 30% of original motor neurons.
- Each motor neuron increases the number of muscle fibers under its control.
- Greater muscle tension (strength) can be generated by increasing firing rates, an inefficient process.
- Each surviving motor neuron now has increased metabolic demands.



Source: Arash Salardini, José Biller: *The Hospital Neurology Book*
www.neurology.mhmedical.com

Viral motor neuron diseases in the 21st century

- Poliomyelitis in unvaccinated individuals:
  - Amish communities in North America
  - 3rd world countries, particularly where fundamentalist religions hold sway.
  - Herd immunity is extremely high but risk exists of re-emergence of infection related to vaccine opposition.
- Vaccine-related paralytic polio:
  - Vanishingly rare in the individual being vaccinated.
  - May occur in unvaccinated individuals caring for a recently vaccinated infant (e.g., grandparents, nannies)
- Arbovirus-related anterior horn cell diseases:
  - West Nile virus
  - Zika virus
  - [Chikungunya, dengue, Japanese encephalitis]
- As-yet unidentified acute, epidemic paralytic illnesses (recent outbreak in children in the US).

Late effects of paralytic polio (post-polio syndromes)

- Some individuals with paralytic polio recover partially or completely only to experience annoying or even disabling symptoms years or decades later, after a long period of stability.
- Most common is "*post-polio syndrome (PPS)*".
- Much less common but more serious is *"post-polio muscular atrophy (PPMA)"*.
- In Australasia the terminology is different:
  - PPS is referred to as LEoP; i.e., *L*ate *E*ffects *o*f *P*olio.
  - PPMA is referred to as PPS.

Late effects of paralytic polio (post-polio syndromes)

- These disorders affect between 25% and 50% of individuals who have had paralytic polio; i.e., there may be up to 6000 people in NZ living with one of the post-polio syndromes.
- There is no reliable estimate of the number of people in NZ who suffer from these syndromes.
- The likelihood of developing one of these disorders is directly proportional to the severity of the initial episode of polio and the degree of initial recovery.
- An identical syndrome occurs in survivors of other paralytic diseases (GBS) and even following nerve injury (brachial plexus).

Post-polio syndrome (LEoP)

- Can occur in individuals and in body regions that *appear* to have made a complete recovery from the initial attack.
- Primary manifestation is fatigue which can be severely disabling.
- Associated pain in muscles, tendons, ligaments and joints is a common accompaniment.
- Depression is also common.
- Progressive muscle weakness does not occur but stamina is poor; i.e., ability to sustain tasks is diminished.

Post-polio syndrome (LEoP)

- Probably an over-use phenomenon:
  - Everyday activities are harder to perform because of the depletion of the motor neuron pool and increased metabolic demand on surviving motor neurons leading to fatigue.
  - Joint and ligament instability due to weakness, even if mild or subclinical, may lead to micro-injuries to soft tissues and arthritic changes in the joint (accelerated osteoarthritis).

Post-polio syndrome (LEoP)

Management:

- Acknowledge that the condition exists.
- Fatigue management:
  - Ensure that there are no co-morbidities that could be contributing to fatigue (anemia, diabetes, hypothyroidism, sleep apnoea, hypoxia from hypoventilation due to weak respiratory muscles)
  - Weight management.
  - Maintain physical activity.
  - Regular but light aerobic exercise – “little and often”.
  - Energy conservation.
  - Judicious use of stimulants is controversial:
    - SSRI’s and SNRI’s are mild stimulants and can be very useful.
    - Modafinil (Provigil), methylphenidate (Ritalin) and dextroamphetamine (Adderall) can be safely used and this is often done in the US but I have never seen it done in NZ.

Post-polio syndrome (LEoP)

Management:

- Pain management:
  - Physical maneuvers such as stretching, massage and light exercise.
  - Swimming can be particularly useful but beware cold water – cold can make symptoms worse (cf; MS-related fatigue).
  - NSAIDs have some benefit but need to be used judiciously to avoid chronic AE's.
  - Avoid opioids.

Post-polio syndrome (LEoP)

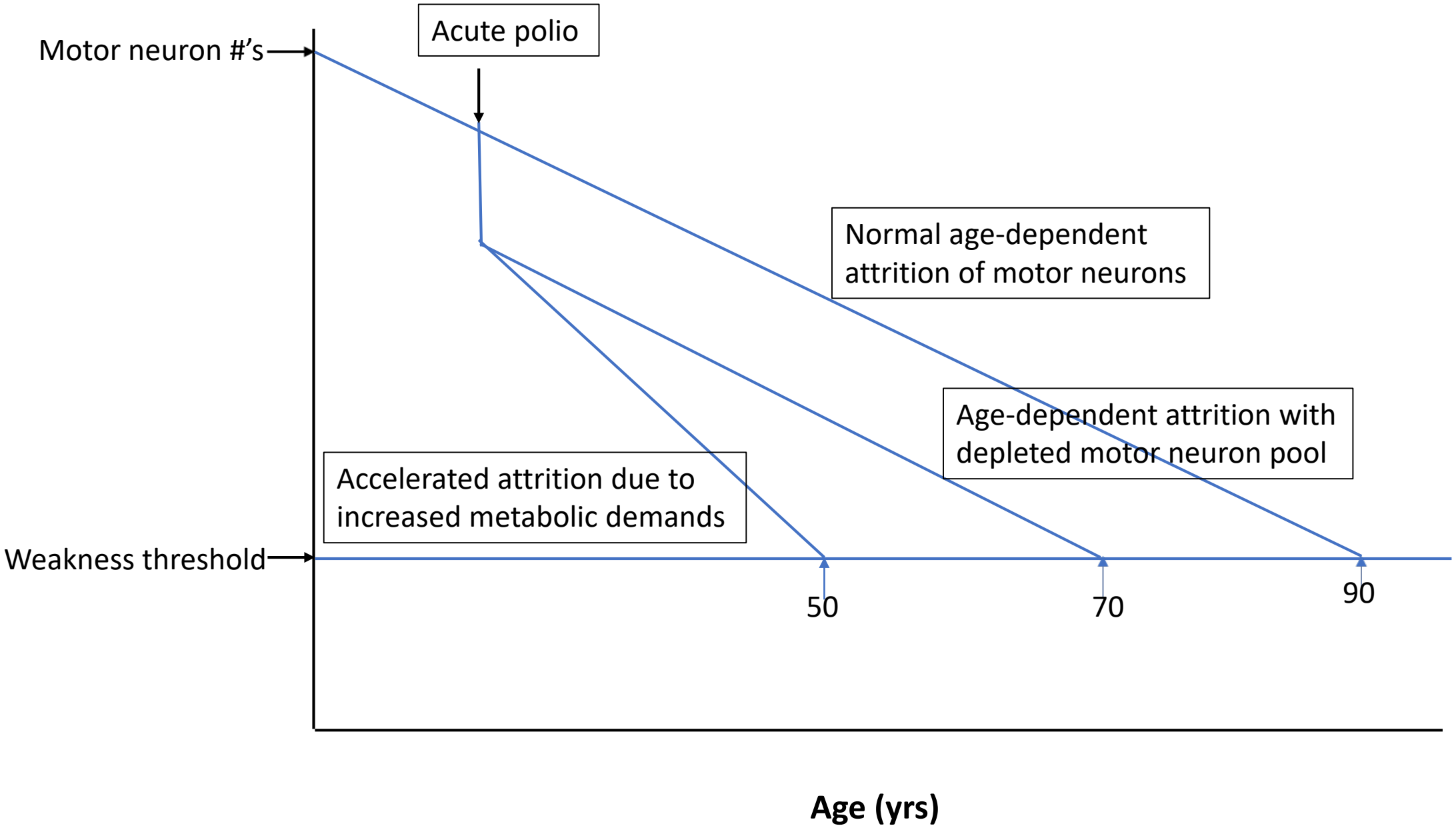
- Pain management (cont'd):
  - Although the pain is not thought to be neuropathic, medications that typically help neuropathic pain also help PPS pain:
    - TCA's (but tend to exacerbate fatigue).
    - AED's (particularly gabapentin and pregabalin)
    - SNRI's (but not SSRI's)
    - Cannabinoids – role not established but preliminary results in other pain states are encouraging.
    - Combinations to harness additive beneficial effects without additive AE's; e.g., GBP (sedative) + SNRI (stimulant).
  - Non-traditional/complementary treatments:
    - Acupuncture
    - Massage
    - Meditation
    - Etc, etc, etc.

Post-polio muscular atrophy (PPMA)

- Usually associated with the less specific PPS (LEoP) symptoms.
- Additional *progressive* muscle weakness.
- Weakness restricted to muscles that had incompletely recovered from the initial attack [?].
- Manifestations depend on body region involved:
  - Dysphagia, dysarthria and dysphonia.
  - Respiratory difficulties, particularly nocturnal hypoventilation.
  - Limb weakness.
- May be mistaken for ALS but:
  - No UMN involvement.
  - Pace of progression much slower.

Post-polio muscular atrophy (PPMA)

- Pathogenesis:
  - Age-related attrition of a depleted motor neuron pool.
  - Accelerated attrition of a depleted motor neuron pool due to increased metabolic demands.
  - Inflammatory reaction in motor neuron pool.


Motor neuron #'s
Acute polio
Normal age-dependent attrition of motor neurons
Age-dependent attrition with depleted motor neuron pool
Accelerated attrition due to increased metabolic demands
Weakness threshold
50
70
90
Age (yrs)

Post-polio muscular atrophy (PPMA)

Management:

- Management of PPS symptoms.
- Assistive devices.
- Speech and swallowing therapy to improve communication and promote safe eating and to protect the airway:
  - Consider PEG if weight loss is excessive.
- Respiratory support (BiPAP).

Prognosis:

- Progression is usually very slow.
- Increasing disability but not life-threatening unless bulbar and respiratory functions are affected.

Post-polio muscular atrophy (PPMA)

Management – is there a role for immunotherapy?

- It has been suggested that anterior horn inflammation may cause or contribute to accelerated motor neuron degeneration.
  - Sparse autopsy support for this concept.
  - Rationale that residual polio virus AA sequences sustain a chronic immune response is not really plausible.
  - An identical syndrome can occur following other nerve damage; e.g., GBS, traumatic nerve injury.

Post-polio muscular atrophy (PPMA)

Management – is there a role for immunotherapy?

- Results of phase II clinical trials with IVIg purported to show some benefit.
- An international, multi-center phase III clinical trial is currently recruiting subjects (clinicaltrials.gov).
- From a practical perspective it is not possible to use IVIg for this purpose in NZ.
- The risks of chronic use of other immunosuppressive regimens outweigh any benefit.

Late effects of paralytic polio (post-polio syndromes)

- PPS (LEoP) is common, affecting perhaps as many as 50% of individuals.
- PPMA (PPS) is much less common but more disabling, even life-threatening.
- These phenomena also occur as late effects of other acute paralytic illnesses.
- Sufferers from these phenomena express enormous frustration at the lack of awareness, even dismissive attitude from some healthcare professionals.
- Quality of life can be enhanced by aggressive management of these late effects.