

Acute Flaccid Paralysis

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- ⚙ Acute flaccid paralysis (AFP) is a clinical syndrome characterized by rapid onset of weakness, including (less frequently) weakness of the muscles of respiration and swallowing, progressing to maximum severity within several days to weeks.
- ⚙ The term "flaccid" indicates the absence of spasticity or other signs of disordered central nervous system motor tracts such as hyperreflexia, clonus, or extensor plantar responses

- ⚙ AFP is a complex clinical syndrome with a broad array of potential etiologies.
- ⚙ Accurate diagnosis of the cause of AFP has profound implications for therapy and prognosis.
- ⚙ If untreated, AFP may not only persist but also lead to death due to failure of respiratory muscles.

- ⊗ AFP, a syndrome that encompasses all cases of paralytic poliomyelitis, also is of great public health importance because of its use in surveillance for poliomyelitis in the context of the global polio eradication initiative.

Clinical Approach AFP

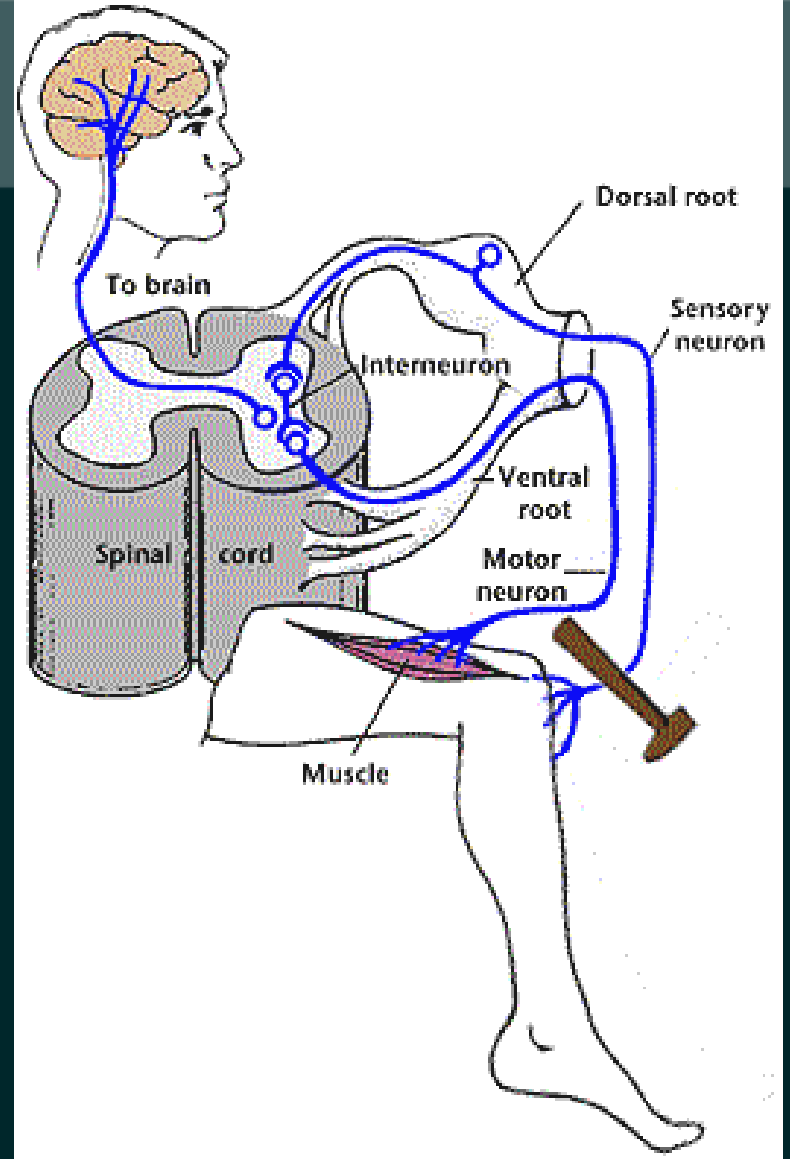
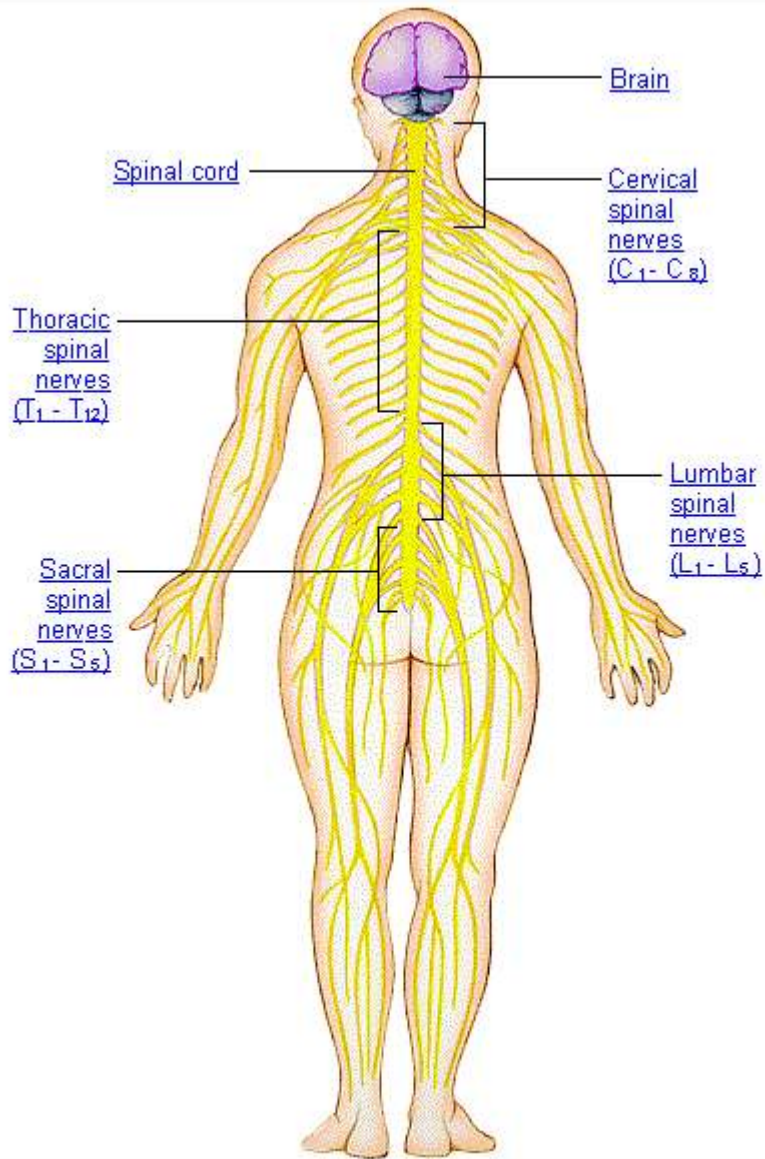
- ⚙ Each case of AFP is a clinical emergency and requires immediate examination.
- ⚙ For all cases, a detailed clinical description of the symptoms should be obtained, including fever, myalgia, distribution, timing, and progression of paralysis.
- ⚙ The symptoms of paralysis may include gait disturbance, weakness, or troubled coordination in one or several extremities

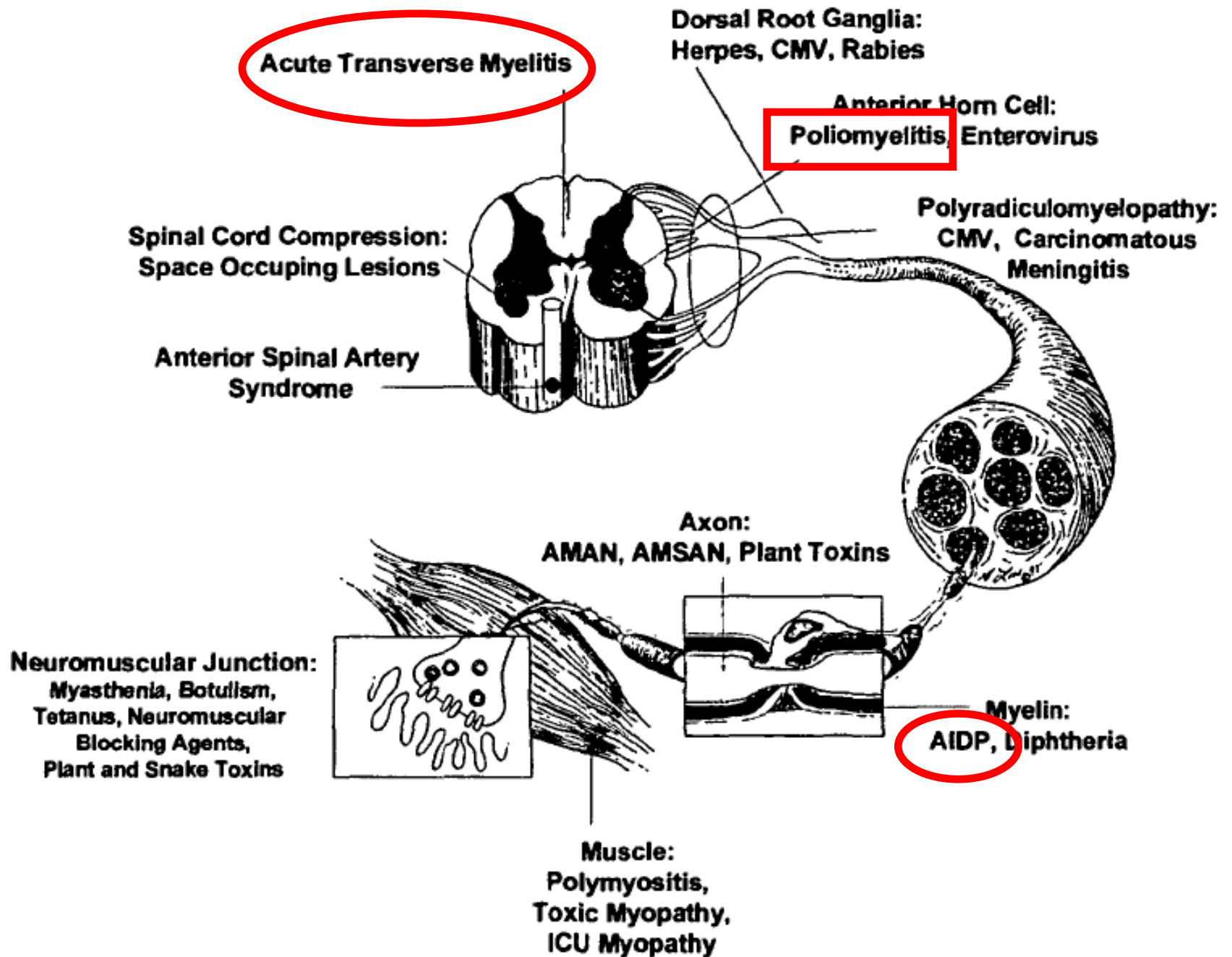
Clinical Approach

- ⚙ Comprehensive neurologic examination, including assessment of muscle strength and tone, deep tendon reflexes, cranial nerve function, and sensation
- ⚙ Look for meningismus, ataxia, or autonomic nervous system abnormalities (bowel and bladder dysfunction, sphincter tonus, neurogenic reflex bladder)
- ⚙ Fasciculation is often cited as a sign of anterior horn cell damage, but it may also be present in demyelinating neuropathies.

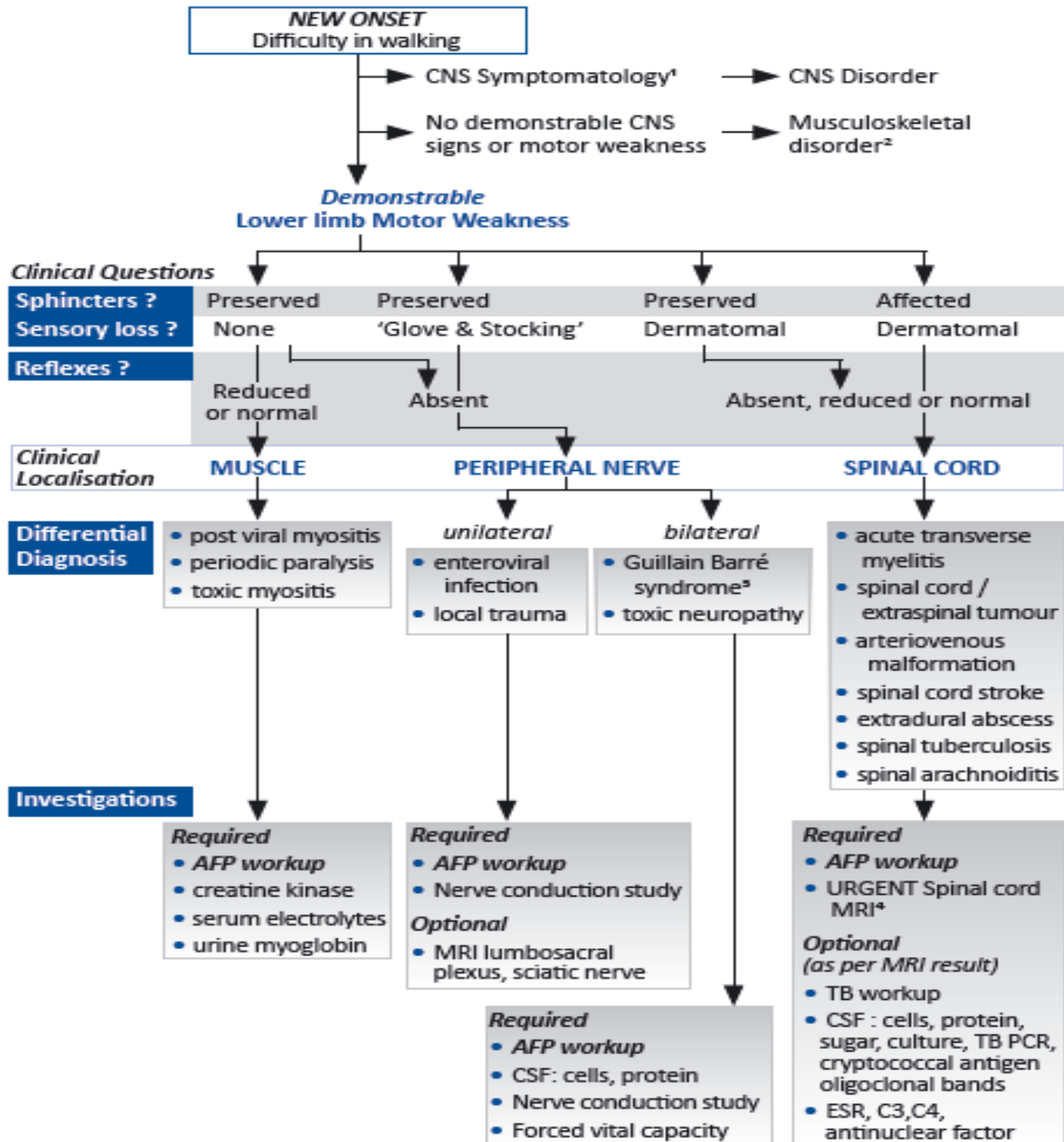
Clinical Approach

- ⚙ Electrophysiologic studies are very important for determining the diagnosis and prognosis of lower motor neuron disease
- ⚙ Nerve conduction velocity and electromyographic studies are used to differentiate demyelinating neuropathies from axonal neuropathies





Clinical Pathways for AF



Guillain–Barre Syndrome (GBS)

- ☼ Guillain–Barre syndrome: the commonest cause of acute flaccid paralysis (AFP) in healthy children
- ☼ 0.9–1.5 per 100,000 population <15y
- ☼ Acute inflammatory demyelinating polyradiculoneuropathy (AIDP)
- ☼ *Symmetrical* progressive *ascending* weakness, *areflexia*, variable sensory complaints, and *elevated CSF protein without pleocytosis*

Pathophysiology of GBS

- ✧ Acquired, monophasic
- ✧ Immune mediated disease
- ✧ No known genetic factor
- ✧ Two thirds of cases follow a respiratory or gastrointestinal infection
 - ✧ Campylobacter infection is the most common, but other organisms include CMV, EBV, HSV, enteroviruses, ...

Pathophysiology of GBS.

- ⊗ The main lesions are acute inflammatory demyelinating polyradiculoneuropathy, with acute axonal degeneration in some cases, particularly those following campylobacter infection
- ⊗ A variety of autoantibodies to gangliosides have been identified especially with axonal forms of the disease

Clinical Features of GBS

- ☼ Two to four weeks after a benign febrile illness
- ☼ Common presentations are paresthesias in the fingers and toes, pain is a common presentation in children (79%), particularly low back pain
- ☼ Symmetrical weakness in the lower extremities, that ascends over hours to days to involve the arms, and in severe cases respiratory muscles

Clinical Features of GBS

- ⊗ Cranial nerves are affected in 30% of the cases, most commonly the facial nerve with bilateral facial weakness
- ⊗ More than 90% of patients reach the nadir of their function within 2–4 weeks

Physical Examination in GBS

- ⊗ Symmetrical weakness with diminished or absent reflexes
- ⊗ Vibration and position sensation are affected in 40% of cases
- ⊗ 50% of patients have evidence of autonomic dysfunction
 - ⊗ Cardiac dysrhythmias
 - ⊗ Orthostatic hypotension, hypertension
 - ⊗ Paralytic ileus
 - ⊗ Bladder dysfunction

Diagnosis of GBS

- ⚙ Cerebrospinal fluid:

- ⚙ After the first week of symptoms, CSF typically reveals normal pressure, *normal cell count, and elevated protein*

- ⚙ Electrophysiologic studies:

- ⚙ Most specific and sensitive tests for diagnosis

- ⚙ Evidence of evolving multifocal demyelination

- ⚙ Normal studies after 10 days of illness make the diagnosis of GBS unlikely

GBS Management

- ⚙ Expectant with mild cases
- ⚙ Immune modulatory therapy for rapidly progressive cases, most effective the first 10 days
 - ⚙ Plasmapheresis
 - ⚙ IVIG
- ⚙ Steroids are not effective and not indicated
- ⚙ Critical care monitoring
 - ⚙ *Most common cause of death is autonomic dysfunction*
 - ⚙ *Second most common cause of death is respiratory failure*

GBS Management

- ⊗ Risk factors for respiratory failure in GBS
 - ⊗ Cranial nerve involvement
 - ⊗ Short time from preceding respiratory illness
 - ⊗ Rapid progression over less than 7 days
 - ⊗ Elevated CSF protein in the first week
 - ⊗ Severe weakness
 - ⊗ Unable to lift elbows above the bed
 - ⊗ Unable to lift head above the bed
 - ⊗ Unable to stand

Prognosis of GBS In Children

- ⊗ Children have a shorter clinical course than adults
- ⊗ Severity of the illness does not correlate with long term outcome, 85% of children have excellent recovery
- ⊗ 50% are ambulatory by 6 months, 70% walk within a year of onset of the disease

Transverse Myelitis

- ⚙ Acute demyelinating disorder of the spinal cord that evolves over days usually but may have a hyperacute presentation
- ⚙ May be associated with demyelination in other parts of the central nervous system
- ⚙ Commonly preceded by a viral infection or immunization

Transverse Myelitis

- ⊗ Commonly presents with an ascending weakness
- ⊗ Initially reflexes may be depressed or absent because of spinal shock or involvement of the nerve roots
- ⊗ Must be considered in cases of weakness without bulbar involvement

Transverse Myelitis

- ⊗ Mean age of onset is 9 years
- ⊗ Symptoms progress rapidly, peaking within 2 days
- ⊗ Usually level of myelitis is thoracic
- ⊗ Sensory level, asymmetrical leg weakness, and early bladder involvement. Back pain is common at the onset
- ⊗ Tendon reflexes may be decreased or increased
- ⊗ Recovery usually begins after a week of onset

Transverse Myelitis

- ⚙ Diagnosis: MRI of the spine usually shows swelling of the cord, but at times is normal. Exclusion of acute cord compression is essential



TM – Treatment and Prognosis

- ⊗ High doses of IV steroids (methylprednisolone) followed by tapering doses of prednisone
- ⊗ Prognosis: 50% make a full recovery, 40% recover incompletely, and 10% do not recover

Enterovirus Infection

- ☼ Poliovirus, coxsackievirus, and the echovirus group are RNA viruses that inhabit the GI tract of humans
- ☼ They are neurotropic, and produce paralytic disease by destroying the motor neurons of the brainstem and spinal cord
- ☼ Poliovirus causes the most severe paralysis, coxsackie and echoviruses are more likely to cause an aseptic meningitis

Non-Polio eneterovirus

- ⊛ *Nonpolio enteroviruses hav* been associated with polio-like paralytic disease, frequently accompanied by other clinical syndromes, such as aseptic meningitis, hand-foot-and-mouth disease, and acute hemorrhagic conjunctivitis.
- ⊛ Among all known nonpolio enteroviruses, enterovirus 71 has been most strongly implicated in outbreaks of central nervous system disease and AFP.

Poliomyelitis – history



- ⚙ Known since ancient Egyptian times
- ⚙ English physician Michael Underwood in 1789, refers to polio as "a debility of the lower extremities"
- ⚙ Poor sanitation contributed to increased natural immunities among human population
- ⚙ Outbreaks started to occur in 20th century

Polio – History

- ⚙️ Outbreaks reached pandemic proportions in Europe, North America, Australia, and New Zealand during the first half of the 20th century.
- ⚙️ In US, 1952 polio epidemic became the worst outbreak in the nation's history.
- ⚙️ Of nearly 58,000 cases reported that year 3,145 died and 21,269 were left with mild to disabling paralysis.
- ⚙️ Intensive care medicine has its origin in the fight against polio



Poliomyelitis – Clinical

- ⊗ Epidemics usually occur in the spring and summer
- ⊗ Usually a brief illness characterized by fever, malaise and GI symptoms precedes the paralytic illness
- ⊗ After the febrile illness, there is a brief period of apparent well being, after which the fever recurs, with headache, vomiting and meningeal irritation

Poliomyelitis – Clinical

- ⚙ Pain in the limbs and spine is followed rapidly by limb weakness
- ⚙ Pattern of limb weakness is variable, but is generally asymmetric
- ⚙ Weakness, diminished reflexes and *muscle atrophy* are seen
- ⚙ Paralysis

Poliomyelitis – Clinical

- ⚙ Bulbar polio may occur with or without spinal polio and is life threatening
 - ⚙ Affected children have prolonged periods of apnea and require mechanical ventilation
 - ⚙ Extraocular muscles are spared
- ⚙ Paralytic polio is rarely seen after the introduction of the polio vaccine

Poliomyelitis

⚙️ Diagnosis:

- ⚙️ Clinical suspicion
- ⚙️ CSF leukocytosis is seen the acute phase, elevated protein may also be seen
- ⚙️ CBC shows leukocytosis
- ⚙️ Virus recovery from stool is essential
 - ⚙️ Obtain stool, blood and throat samples for viral serology, demonstrating a four fold rise in IgG is helpful but not always easy. Positive IgM antibodies is diagnostic

Poliomyelitis

- ⚙ Treatment: mainly supportive
 - ⚙ Mechanical ventilation may be needed in bulbar involvement
 - ⚙ Pain management for paresthesias
 - ⚙ Physical therapy

Polio Vaccine

- ⚙ The early 20th century epidemics—which left thousands of children and adults paralyzed—provided the impetus for a "Great Race" towards the development of a vaccine.
- ⚙ Developed in the 1950s, polio vaccines are credited with reducing the global number of polio cases per year from many hundreds of thousands to around a thousand

Polio Vaccine

- ⚙ 1950 – Koprowsky introduced live attenuated vaccine
- ⚙ 1952 – Salk developed The Salk vaccine, or inactivated poliovirus vaccine (IPV), based on poliovirus grown in a type of monkey kidney tissue culture (Vero cell line), which is chemically inactivated with formalin.
- ⚙ After two doses of IPV (given by injection), 90% or more of individuals develop protective antibody to all three serotypes of poliovirus, and at least 99% are immune to poliovirus following three doses

Polio Vaccine

- ⊗ Albert Sabin developed oral polio vaccine (OPV)
- ⊗ The attenuated poliovirus in the Sabin vaccine replicates very efficiently in the gut, but the vaccine strain is unable to replicate efficiently within nervous system tissue.
- ⊗ A single dose of Sabin's oral polio vaccine produces immunity to all three poliovirus serotypes in approximately 50% of recipients. Three doses of live-attenuated OPV produce protective antibody to all three poliovirus types in more than 95% of recipients.
- ⊗ Human trials of Sabin's vaccine began in 1957, and in 1958 it was selected, in competition with the live vaccines of Koprowski and other researchers, by the US National Institutes of Health and licensed in 1962.

Polio Vaccine

- ⚙ Because OPV is inexpensive, easy to administer, and produces excellent immunity in the intestine (which helps prevent infection with wild virus in areas where it is endemic), it has been the vaccine of choice for controlling poliomyelitis in many countries worldwide.
- ⚙ 1 case per 750,000 vaccine recipients the attenuated virus in OPV showed risk to revert into a paralytic form.
- ⚙ Most industrialized countries have switched to IPV, which cannot revert, either as the sole vaccine against poliomyelitis or in combination with oral polio vaccine



AFP Surveillance

- ⚙ Collecting stools for enterovirus in children with AFP is an important part of the Global Polio Eradication Initiative (GPEI)
- ⚙ For Malaysia to remain a polio-free country we need to prove that none of our cases of AFP are caused by poliovirus infection.
- ⚙ The target “background rate” for AFP in the GPEI is 2 per 100,000 children below 15 years old.

Table 1. Protocol for AFP surveillance in Malaysia

Step	Timing	Description
Case Detection	at diagnosis	Follow case definition for AFP
Case Reporting	within 24 hours	Fax forms to 03-2693 8094 (Virology Unit, IMR; Tel no: 03-2616 2677)
Timing of stool specimens	within 2 weeks of onset of paralysis	2 stool specimens collected no less than 24 hours apart
Collection of specimens		Fresh stool, or rectal swabs containing fecal material (at least 8g – size of an adult thumb). Place in a sterile glass bottle
Transport of stools	as soon as able	Maintain a cold chain of 2 - 8 °C. Transport in dry ice if transportation will take > 24 hours Caution: avoid desiccation, leakage; ensure adequate documentation
Follow up of patients	60 days from paralysis	To determine whether there is residual paralysis on follow up

Five-year surveillance of acute flaccid paralysis in Malaysia

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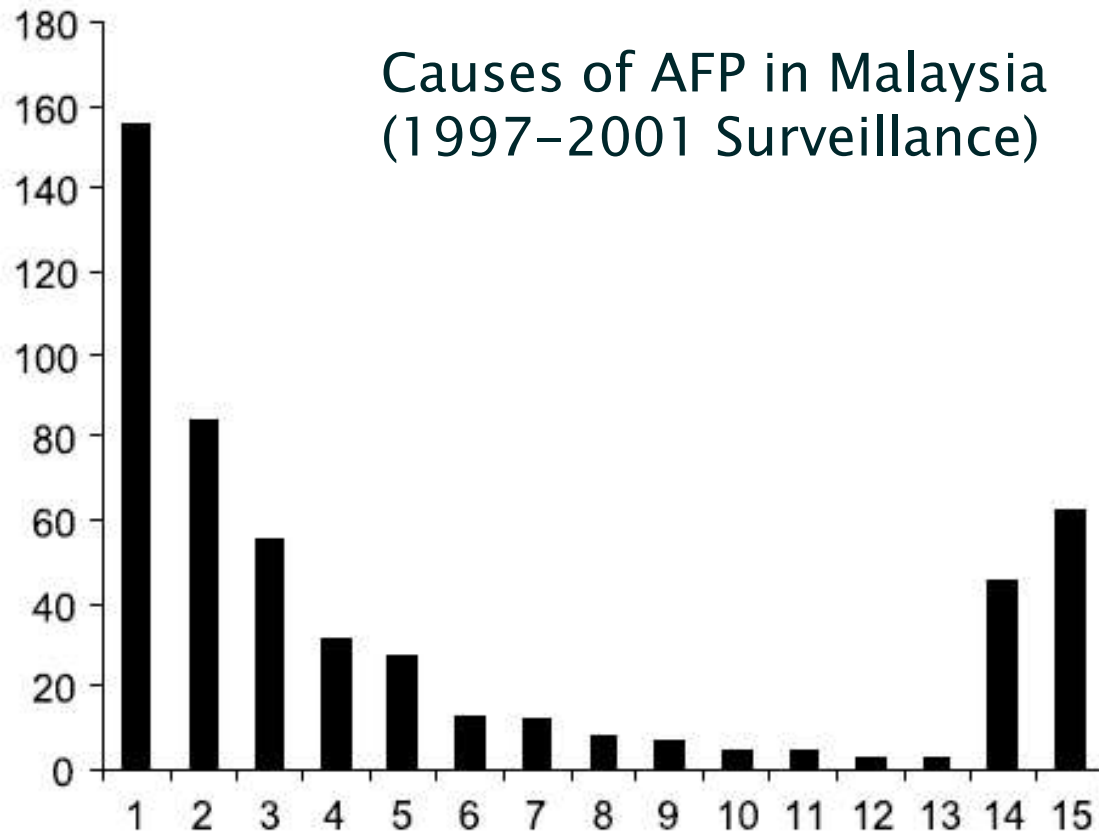
Objective: The nation-wide surveillance for acute flaccid paralysis (AFP) was implemented in Malaysia in 1995 and further intensified in 1996 as part of the World Health Organization's (WHO) certification process for polio eradication in the Western Pacific Region. Clinical data on AFP cases during a 5-year surveillance period from 1997 to 2001 were compiled and analysed.

Results: Based on 517 cases of AFP reported during this 5-year period, the overall rate of AFP was 1.2 per 100 000 children below 15 years old. The major clinical diagnosis associated with AFP were Guillain–Barre syndrome (30.2%), central nervous system infection (16.2%), transverse myelitis (10.6%) non-polio enterovirus infection (6.2%), and hypokalaemic paralysis (5.2%). This unusual pattern with an excess of CNS infection and non-polio enterovirus infection was attributed to the outbreak of enterovirus 71 infection nation-wide in 1997. According to the WHO virological classification, there was no case of poliomyelitis due to wild poliovirus. Three cases were 'polio compatible', there were no cases of vaccine-associated paralytic polio (VAPP), while 62 cases (12.0%) were merely classified as 'non-polio AFP'.

Conclusion: Overall, these data suggest the absence of circulation of wild poliovirus in Malaysia from 1997 to 2001. The pattern of AFP in this study is different from other published reports.

No. of cases

Causes of AFP in Malaysia (1997–2001 Surveillance)



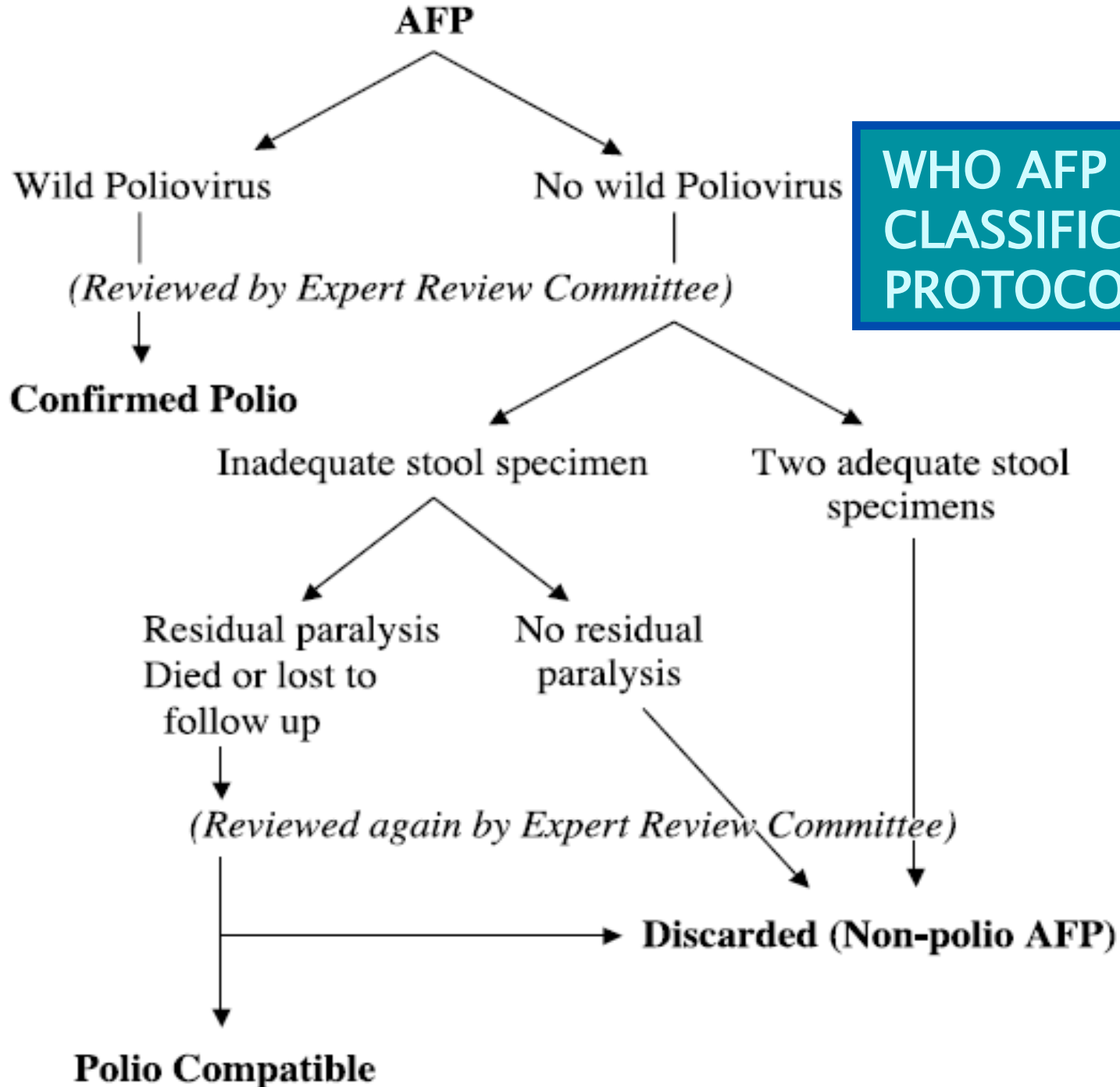
GBS – 30.2%

CNS infections – 16.2%

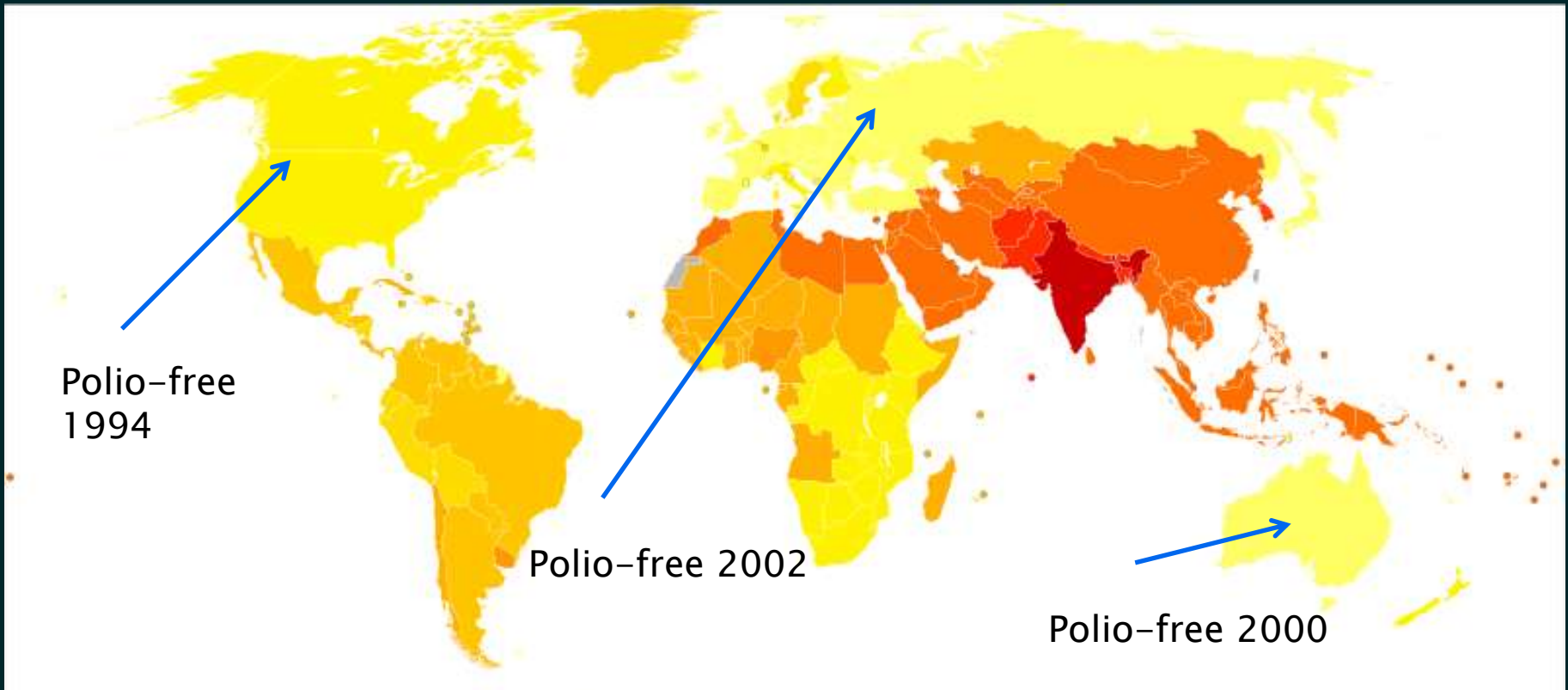
Transverse myelitis – 10.6%

Fig. 2 Causes of acute flaccid paralysis, 1997–2001. Bar 1, Cullain Barré Syndrome ($n = 156$; 30.2%); Bar 2, CNS (central nervous system infection) ($n = 84$; 16.2%); Bar 3, transverse myelitis ($n = 55$; 10.6%); Bar 4, non-polio enterovirus ($n = 32$; 6.2%); Bar 5, hypokalemic paralysis ($n = 27$; 5.2%); Bar 6, viral myalgia/myositis ($n = 13$; 2.5%); Bar 7, spinal cord lesions ($n = 7$; 1.4%); Bar 8, traumatic nerve injury ($n = 8$; 1.5%); Bar 9, acute stroke ($n = 7$; 1.4%); Bar 10, Todd's paralysis ($n = 5$; 1.0%); Bar 11, acute cerebellar ataxia ($n = 5$; 1.0%); Bar 12, 'polio compatible' ($n = 3$; 0.6%); Bar 13, botulism ($n = 3$; 0.6%); Bar 14, miscellaneous ($n = 45$; 8.7%); Bar 15, unclassified ($n = 62$; 12.0%).

**WHO AFP
CLASSIFICATION
PROTOCOL**



Age-standardised disability-adjusted life year (DALY) rates from Poliomyelitis by country (per 100,000 inhabitants) – 2002



Thank You