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REVIEW ARTICLE

Practical approach to the child presenting with acute generalised weakness

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Key Points

1 Acute generalised muscle weakness in children is a paediatric emergency.
2 The differential diagnosis is broad and clinical localisation of the lesion is paramount.
3 A careful history and neurologic examination guide timely investigations and management.

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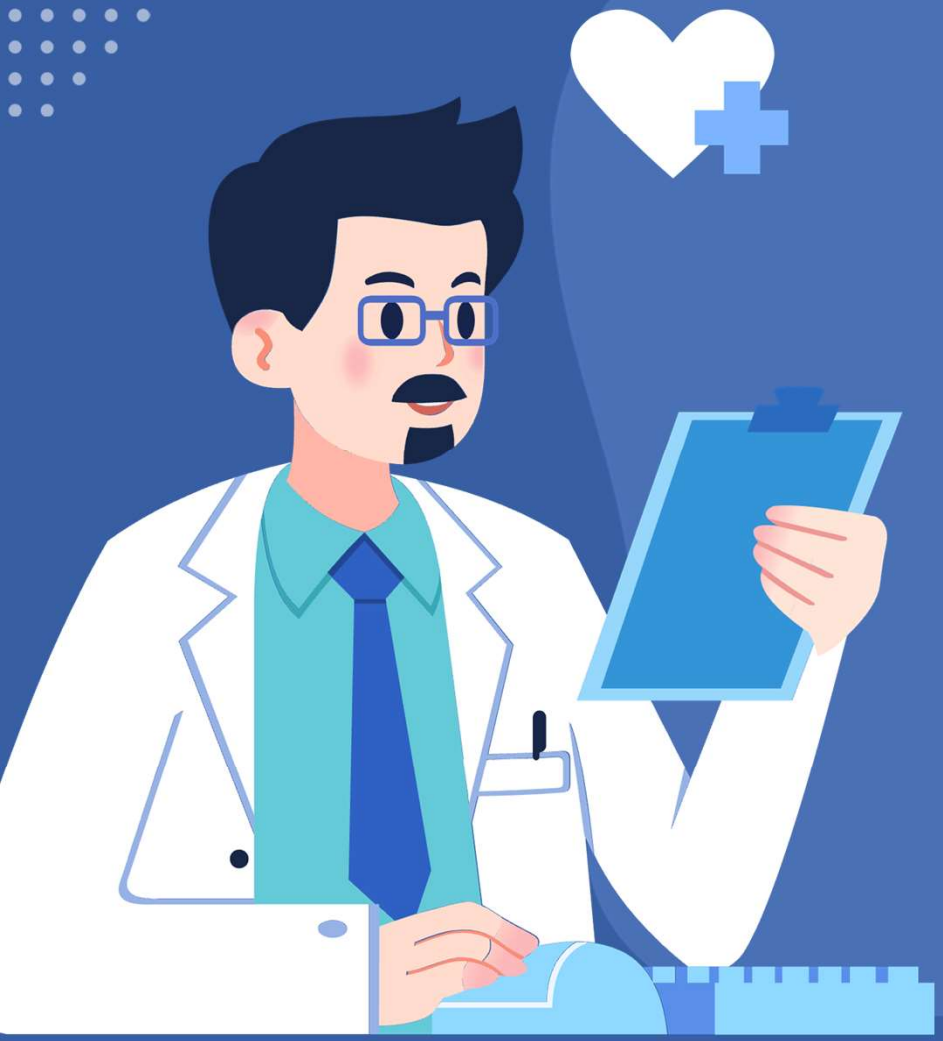
Conflicts of interest: None.

Practical approach to the child presenting with acute generalized weakness.

Acute onset generalized muscle weakness in a child is a pediatric emergency. It is characterized by rapid onset muscle weakness which reaches maximum severity within ٣–٤ weeks, and usually within several days.

Acute flaccid paralysis is defined by the WHO as rapid onset of weakness progressing to maximum severity within ١ to ١٠ days. The term ‘flaccid’ is used to indicate the absence of spasticity or other upper motor neuron signs such as hyper-reflexia, clonus, or extensor plantar responses.



Children commonly present with difficulty walking, standing or sitting.

Muscle weakness usually affects the lower limbs and may also involve the trunk, upper limbs and face.

The differential diagnosis is broad and clinical localization of the lesion within the central and/or peripheral nervous system (‘where is the lesion?’) is paramount when considering differential diagnoses and timely investigation and management.

We review some of the more common pathologies causing acute generalized muscle weakness in children, with a focus on pathology affecting the spinal cord and lower motor neuron rather than acute cerebral pathology such as acute ischemic stroke where the pattern of weakness (e.g. hemiparesis) is usually distinguishable from more generalized weakness or paraparesis.

Overall Approach to Acute Generalized Weakness

Important aspects of the **clinical history** include but are not limited to :

(i) the location and pattern of weakness (e.g. proximal versus distal muscles, involvement of cranial nerves or respiratory muscles);

(ii) the time course and progression of the weakness;

(iii)associated sensory changes or bowel and bladder disturbance;

(iv) any prior episodes;

(v) recent illnesses or vaccinations; and

(vi) relevant family history

From a neuroanatomy perspective, spinal cord lesions result in upper motor neuron signs whilst lower motor neuron lesions (lesions in the anterior horn cell, peripheral nerve, neuromuscular junction or muscle) result in lower motor neuron signs. It is important to remember that whilst the *anterior horn cell* is physically *located in the spinal cord*, it is part of the lower motor neuron and lesions in this location result in lower rather than upper motor neuron signs.

Table 1 Causes of acute generalised weakness

Location of lesion	Examples
Spinal cord	**Transverse myelitis**
	Spinal cord infarction
	Fibrocartilaginous embolism
	Compressive myelopathy, e.g. haemorrhage, tumour
	Traumatic spinal cord injury, e.g. non-accidental injury
	Discitis
Anterior horn cell	**Acute flaccid myelitis** (e.g. enterovirus EV71, other neurotropic viruses)
	Acute poliomyelitis, vaccine associated poliomyelitis
Peripheral nerve	**Guillain–Barré syndrome**
	Neuropathies of infectious diseases
	Acute toxic neuropathies (e.g. heavy metals)
	Acute intermittent porphyria
Neuromuscular junction	**Myasthenia gravis**
	Botulism
	Tick bite paralysis
	Congenital myasthenic syndromes
	Lambert Eaton myasthenic syndrome
	Toxin mediated, e.g. snake bite, organophosphate poisoning
Muscle	**Benign acute childhood myositis**
	Viral myositis
	Dermatomyositis
	Periodic paralyses
	Rhabdomyolysis
	Metabolic disorders, e.g. mitochondrial disorders
	Drug-induced paralysis
Systemic Disease	Critical illness neuropathy/myopathy
Other	**Functional neurological disorder**

Table 2 Lesion localisation in acute onset muscle weakness

	Spinal cord	Anterior horn cell	Peripheral nerve	Neuromuscular junction	Muscle
Tone	Increased†	Decreased	Decreased	Normal/decreased	Normal/decreased
Distribution	Paraparesis, quadriparesis	May be asymmetrical/ monoplegia Proximal > distal	Distal > proximal	Cranial nerves Proximal > distal	Proximal > distal
Reflexes	Increased†	Decreased/absent	Decreased/absent	Normal/decreased	Normal/decreased
Plantar responses	Extensor†	Flexor	Flexor	Flexor	Flexor
Other	Sensory level Sphincter dysfunction	Fasciculation/atrophy	Sensory abnormalities May have autonomic dysfunction	Fatigability Ptosis Ophthalmoplegia	Muscle pain; atrophy or hypertrophy

† In the hyperacute phase of spinal cord pathology (often referred to as 'spinal shock'), hypotonia, hyporeflexia and absent extensor plantar responses may predominate, and later evolve into upper motor neuron signs.

Different causes of peripheral weakness ;

Transverse Myelitis:

Acute transverse myelitis (ATM) is an inflammatory demyelinating disorder of the spinal cord with a range of etiologies that include idiopathic acute transverse myelitis, neuromyelitis optica spectrum disorder, myelin oligodendrocyte glycoprotein antibody disease, multiple sclerosis and other rheumatologic diseases such as systemic lupus erythematosus.

Children with transverse myelitis present with acute onset (progression to nadir between ۴ h and ۲۱ days) motor, sensory and/or sphincter dysfunction.

A preceding infection is reported.(٢/٣ of children in the ٤ weeks prior to symptom onset).
Weakness is usually bilateral and often severe, affecting the lower limbs and there may also be involvement of the upper limbs depending on the extent of spinal cord involvement.
Sensory level :this may be hard to determine in younger children.

Bladder and bowel disturbance in the form of urinary retention and constipation are common with acute sphincter dysfunction reported in up to ٨٠%–٩٠% of children with ATM.

Most children with ATM have upper motor neuron signs with increased tone, clonus and/or hyperreflexia with extensor plantar responses however in the ***very acute phase***, **hypotonia and areflexia** may predominate and later evolve into upper motor neuron signs.

Examination for a palpable bladder and urinary retention is important from a diagnostic and management perspective.

The main differential diagnoses of ATM include an acute compressive myelopathy (such as a spinal cord hemorrhage) or spinal cord infarct, although the time course of these is usually hyperacute and less than the ۴-h time frame specified in the diagnostic criteria for ATM.

ATM can also occur as part of acute disseminated encephalomyelitis, another demyelinating disorder common in childhood, defined by the presence of encephalopathy and polyfocal neurologic deficits attributable to the brain or spinal cord.

Evidence of unilateral or bilateral optic neuritis (e.g. reduced visual acuity and pain on eye movement) also provide clues to a demyelinating etiology.

Diagnosis:

Based on Hx & NE then urgent neuroimaging of the spinal cord with MRI,

Concurrent imaging of the brain may also indicate other areas of demyelination and assist in determining the etiology of the of the ATM.

Acute Flaccid Myelitis:

A polio-like condition that primarily affects children.

It is thought to be driven by epidemics of enteroviral infections, especially A٧١ and D٦٨ subtypes.

Most patients have a prodromal illness with fever, respiratory symptoms, and occasionally gastrointestinal symptoms.

AFM is characterized by acute onset of flaccid weakness in one or more limbs, with hyporeflexia or areflexia in the affected limb. Weakness is often asymmetric, upper limbs are affected more often than lower limbs, and sensation is intact.

Truncal, neck, respiratory, bulbar, facial and extraocular muscles can also be affected.

Spine MRI :T٢ signal abnormality in grey matter/anterior horn cells of the spinal cord.

Discitis:

Young child under the age of ٥ years with refusal to weight-bear, walk or crawl, associated with pain or irritability.

Lower limb neurologic examination is often normal, however hypotonia, hyporeflexia and weakness may be present.

Most children with discitis are often apyrexial and have an elevated ESR, with a negative blood culture.

A plain spinal radiograph may be useful if symptoms have been present for more than ١٠ days. Radiograph changes include loss of intervertebral disc height and endplate irregularities.

An MRI spine is recommended to confirm the diagnosis.

Guillain Barré Syndrome (GBS):

An acute inflammatory polyneuropathy and the most common cause of acute flaccid paralysis.

Preceding infection is reported.

Children typically present with bilateral weakness in the lower limbs which progresses to involve the upper limbs and cranial muscles.

The nadir of weakness occurs within ٢٤ h to ٤ weeks, although most children reach maximal disability within ٢ weeks of onset.

Classic pattern of weakness is ‘ascending’, with distal to proximal progression, a pattern of proximally predominant weakness will occur in ۱۵%–۲۰% of patients.

Cranial nerve involvement, particularly facial weakness (which may at times not be picked up on neurologic examination), but also bulbar weakness and ophthalmoplegia can occur in up to ۴۶% of children.

Neuropathic pain and distal paresthesia are frequent and often poorly localized.

Pre-school aged children with GBS may present with non-specific features such as pain, irritability, apparent meningism and refusal to weight bear, resulting in a delayed diagnosis.

key features :

-Bilateral weakness, and absent or decreased deep tendon reflexes.

-A true sensory level is rare and should prompt consideration of spinal cord pathology.

-Autonomic nervous system involvement occurs in about a quarter of children and can cause blood pressure instability, sinus tachycardia, pupillary abnormalities, and irregular sweating.

-Sphincter dysfunction including urinary retention can occur, however is uncommon and should also prompt consideration of spinal cord pathology.

Key investigation findings:

_(CSF) cytoalbuminemic dissociation

_abnormalities on neurophysiologic testing, however

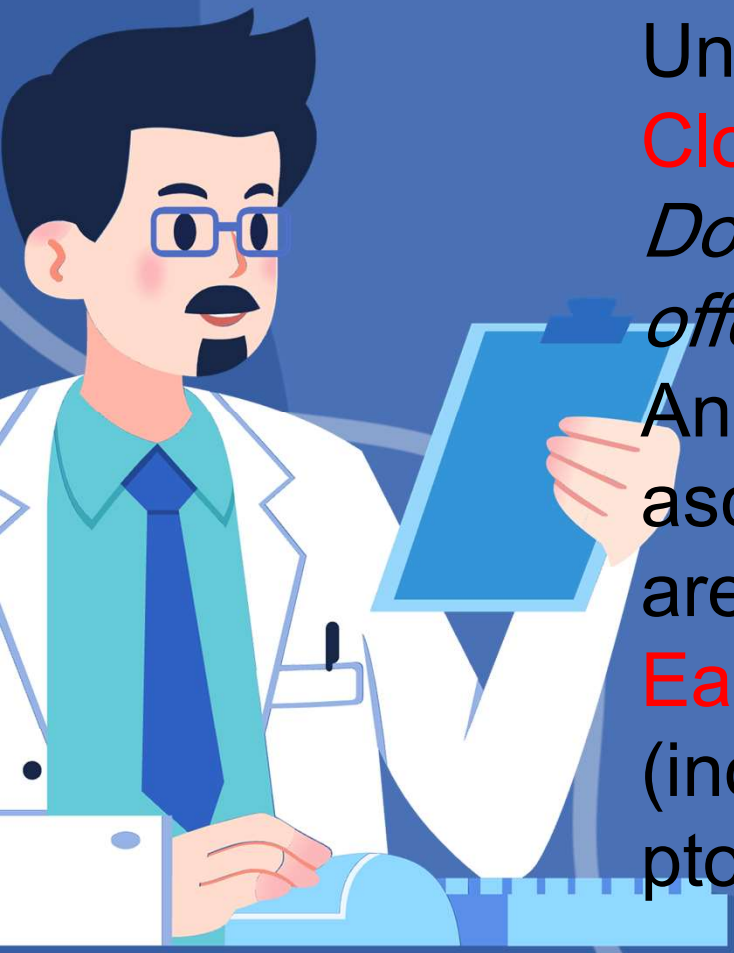
✓ Both can be normal if done early (within ١ week of symptom onset)

_Up to ٩٠% of children with GBS have nerve root enhancement on post contrast spinal cord MRI.

_CPK:Normal

❖ *Benign Acute Childhood Myositis:*

- ❖ Benign acute childhood myositis is a common condition that presents in the context of a prodromal viral illness, classically influenza.
- ❖ Children refuse to walk or have an acute change in gait pattern.
- ❖ Children have prominent calf pain and tenderness to palpation, and creatine kinase levels are elevated in all cases.
- ❖ Muscle strength is normal, and reflexes are preserved.
- ❖ It may be difficult to ascertain if true weakness is present, as pain often limits formal assessment of power.



Tick Paralysis:

Uncommon.

Closely mimics GBS.

Does not respond to any treatment until the offending tick is removed.

An unsteady gait is then followed by ascending symmetrical paralysis and areflexia.

Early cranial nerve involvement is a feature (including reduced gag reflex, facial paralysis, ptosis, mydriasis and loss of ocular motility).

In children with acute flaccid paralysis who live in geographic regions where ticks are endemic, a careful examination for ticks, particularly in the scalp or hairline should be undertaken.

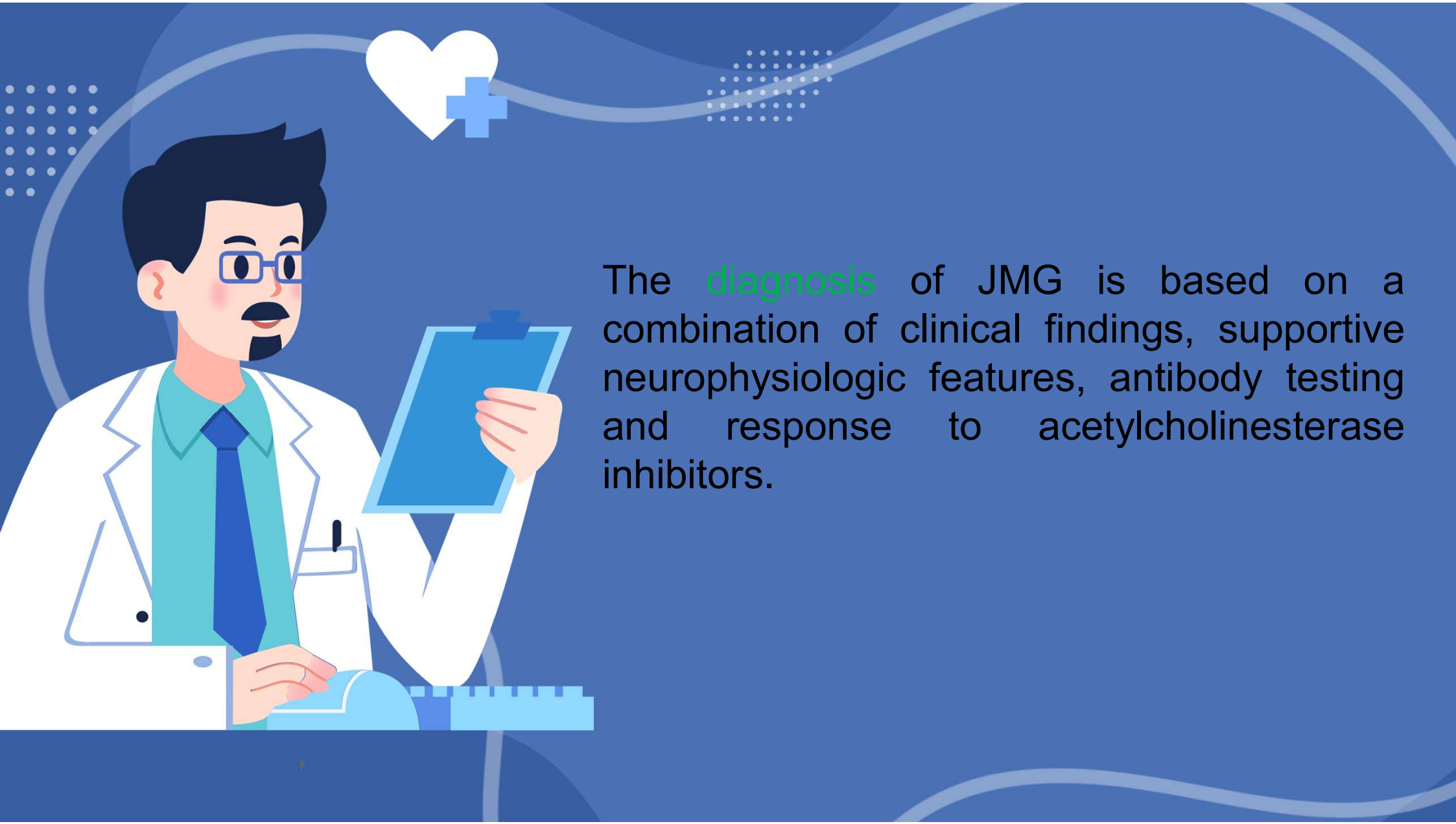
Juvenile Myasthenia Gravis:

Antibodies against the postsynaptic membrane of the neuromuscular junction cause the autoimmune disease myasthenia gravis, which causes muscle weakness with fatigability.

JMG can be ocular or generalized.

In children with generalized JMG, weakness is usually proximally predominant and rapidly fatigable with repeated testing, and is usually associated with ptosis, and unilateral or asymmetric ophthalmoplegia.

Weakness usually worsens over the day and becomes better with rest. Severe cases may present in ‘myasthenic crisis’ with respiratory muscle weakness and respiratory impairment.



The diagnosis of JMG is based on a combination of clinical findings, supportive neurophysiologic features, antibody testing and response to acetylcholinesterase inhibitors.

Congenital myasthenic syndromes are a group of rare inherited neuromuscular junction disorders with genotypic and phenotypic diversity that are not autoimmune and distinct from JMG but share common clinical features.

Children with ***CMS*** are often symptomatic from early in life however can sometimes present with acute hypotonia, ptosis and weakness with bulbar dysfunction and breathing difficulties in the context of respiratory infections.

Infant Botulism:

The spore-forming, anaerobic, gram-positive bacteria Clostridium botulinum, which is prevalent worldwide in soil, produces a neurotoxin that causes infant botulism.

When spores are consumed, an infant's intestinal tract produces and absorbs toxins.

Infant botulism, although rare, is important to recognize because specific treatment with human botulinum antitoxin is available.

Subacute constipation is the initial symptom prior to onset of muscle weakness.

Botulism can affect infants between ۶ weeks and ۹ months of age, with the peak incidence occurring between ۲ and ۳ months of age.

Infants present with hypotonia, generalized weakness, reduced suck, poor feeding, constipation, prominent cranial nerve involvement (such as reduced gag reflex, facial paralysis, ptosis, mydriasis and loss of ocular motility) hyporeflexia and respiratory difficulties.

A definitive diagnosis can be made with the detection of botulinum toxin and the isolation of C. botulinum from stool samples.

Additionally, neurophysiologic studies can support an early diagnosis.

Functional Neurological Disorder:

Functional neurologic disorder (FND) is characterized by abnormal nervous system functioning rather than structural disease and is a common cause of acute weakness in children.

No longer thought of as a ‘diagnosis of exclusion’.

FND is a phenotype-based diagnosis supported by clinical signs that show inconsistency, reversibility, and incompatibility with recognized neurologic conditions.

Some helpful clinical discriminators include Hoover’s sign (hip flexion and extension testing showing inconsistency in attended compared to unattended movement in affected leg), drift without pronation, and collapsing weakness (sudden loss of tone or strength during strength testing).

Clear positive signs of inconsistency of deficits support the diagnosis of FND; it should not be made exclusively based on psychosocial factors, psychiatric comorbidities or negative imaging.

THANK YOU