



The Child Who Trips, Falls, and Can't Keep Up

When Is It More Than Clumsiness?

Recognizing Neurologic Causes of Clumsiness in Children: A Focus on Neuromuscular Disorders

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September 19, 2026



Seattle Children's®

Speaker Disclosures

- **Grants:** Seattle Children's Hospital academic enrichment fund (own research project).
- **Honoraria:** Biogen; Scholar Rock; ITF Therapeutics.
- **Consulting / Advisory Boards:** Regenxbio; Solid Biosciences; Biogen; Scholar Rock; Sarepta Therapeutics; ITF Therapeutics; Johnson & Johnson; Catalyst Pharmaceuticals.
- **Clinical Trials (PI or Sub-Investigator):** Industry-sponsored neuromuscular trials, including Sarepta Therapeutics, Pfizer, Solid Biosciences, Scholar Rock, Biogen, and Catalyst Pharmaceuticals, among others (see CV for full list).
- **Relevant Nonfinancial Relationships:** None.
- **Off-Label Use:** No off-label or investigational medication uses will be discussed.



Learning Objectives

- Recognize when a child who is “clumsy” may have an underlying neurologic disorder.
- Identify red flags in the history and physical examination that should prompt further evaluation.
- Differentiate common causes of falls, gait abnormalities, and exercise intolerance in children.
- Know when to order tests, when to refer, and when to worry.



Roadmap for the Next 50 Minutes

- **Building your differential:** red flags that separate “clumsy” from concerning
- **Central Nervous System:** causes of motor dysfunction
- **Peripheral Nervous System:**
 - **Duchenne muscular dystrophy:** the diagnosis you can't afford to miss
 - **Spinal muscular atrophy:** a newborn-screening success story
 - **Congenital myopathies & congenital myasthenic syndromes:** the floppy infant who doesn't outgrow it
- **Putting it together:** workup, referral, and the role of PT
- **Questions & discussion**



PART 1

Building Your Differential: From “Clumsy” to Concerning



Why “Clumsy” Deserves a Second Look

- Caregivers who express concern about developmental problems are correct more than **80%** of the time
- Delay in diagnosis can lead to delay in treatments and resources
- **Your job isn't to name the diagnosis:** it's to recognize the pattern that doesn't fit “just clumsy” and know when to escalate.
- **Rule of thumb:** regression, asymmetry, or a relevant family history changes everything.





Definitions- hypotonia

Residual
tension in a
muscle at rest

Passive partial
contraction of
the muscles

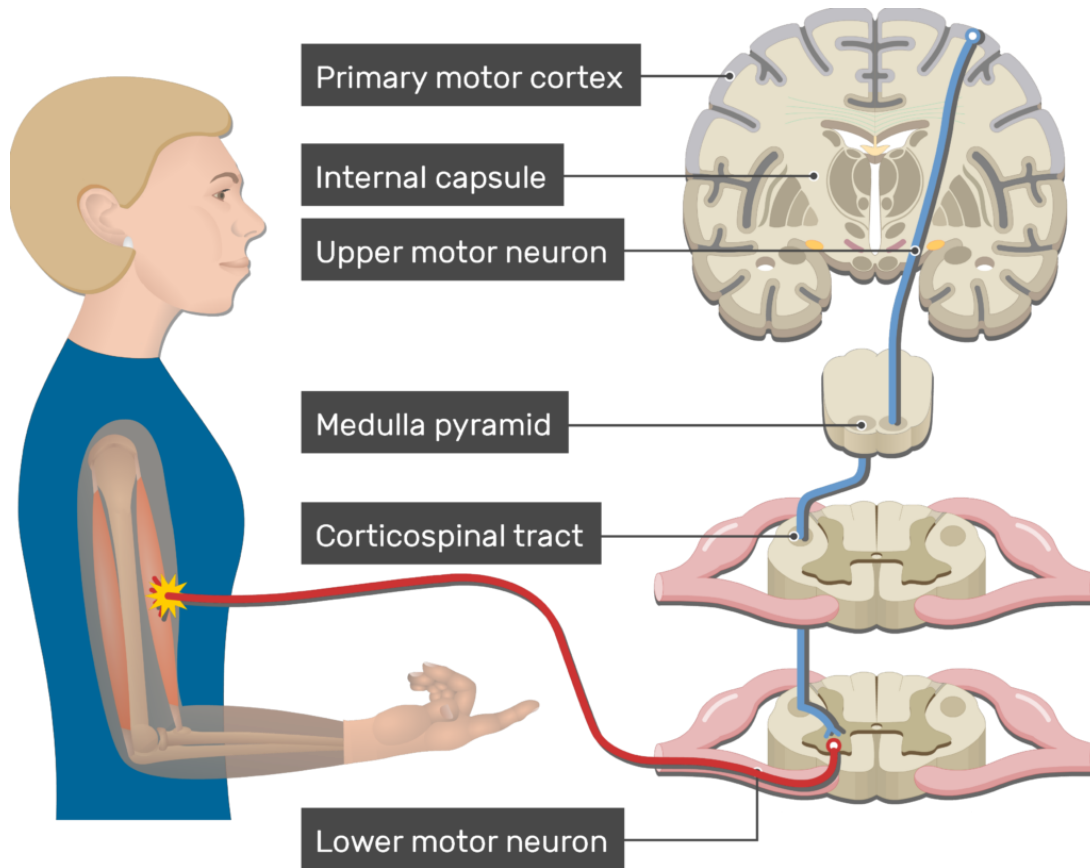
Decrease
resistance of
muscle to
stretch

Floppy baby

How is this
different from
weakness?

Is hypotonia
always
accompanied
by weakness?





Definitions- Weakness

- Decreased ability to voluntarily and actively move muscles against resistance
- Upper motor neuron weakness
- Lower motor neuro weakness



Clinical Evaluation



Prenatal, neonatal and perinatal assessment



Clinical characteristics of muscle hypotonia and weakness



Additional clinical clues to differential diagnosis



Obtaining a History

- **HPI:** fatigability with feeding or activity, slower than peers, difficulty in the playground, frequent tripping or falling , hand preference
- **Pregnancy:** reduced fetal movements, polyhydramnios, or breech presentation can be the first sign of fetal weakness. History of intrauterine drug exposure or maternal diseases
- **Birth/perinatal:** delivery mode, need for resuscitation, and feeding/respiratory status at birth
- **Family history:** ask specifically about consanguinity, muscle disease, stillbirths/unexplained infant deaths, early wheelchair use, and cardiomyopathy
- **Why it matters:** these three histories are fast, free, and often the highest-yield part of the visit — they can shift your differential, and your urgency, before you order a single test.



Developmental Milestones

Age	Motor Milestones
1 month	Lifts head when lying on abdomen
2 months	Holds head up for short periods
3 months	Holds head steady
4 months	Can bear weight on legs, chest up-arm support
5 months	Rolls over in both directions
6 months	Sits without support
9 months	Stand up
10 months	Crawl
12 months	Walks



Red Flags in the History

- Seizures, or any paroxysmal spells
- **Asymmetric hand preference before 12 months of age**
- **Frequent falls, toe-walking, or trouble keeping up with peers**
- Delayed developmental milestones- Walking after 16 months. Other delays
- Fluctuating or fatigable weakness that worsens through the day or with repetitive activity.
- Loss of previously acquired skills (regression) — **never normal**, always investigate.
- **Feeding difficulty, hypotonia, or respiratory issues in infancy**



Red Flags on the Physical Exam

- **Abnormal head growth trajectory** — crossing percentiles
- **Gowers sign** — using hands to “climb up” the legs when rising from the floor: proximal weakness until proven otherwise.
- **Gait-** look at walking and running.
 - Waddling (myopathic) gait, hyperlordosis- proximal weakness
 - Foot drop
 - Hemiplegic gait
- **Ptosis, ophthalmoplegia, or facial weakness** — think neuromuscular junction or myopathy.
- **Asymmetric weakness or reflexes**
- **Hypo or hypertonia**
- **Scoliosis, contractures, or a high-arched palate in an infant**



Localizing the Weakness: A Quick Framework

Level	Tone / Reflexes	Distribution	Extra Clues
Central (brain/cord)	↑ tone, ↑ reflexes	Often asymmetric ± sensory level	Seizures, AMS, bowel/bladder change
Anterior horn cell / nerve	↓ tone, ↓/absent reflexes	Distal ≥ proximal, symmetric	Fasciculations; sensory change if nerve
Muscle	Normal→↓ tone, reflexes preserved until late	Proximal > distal, symmetric	CK often ↑, calf hypertrophy
Neuromuscular junction	Normal tone/reflexes	Fluctuating, ocular/bulbar	Fatigability; CK normal





Resting Tone



**Vertical
Suspension**



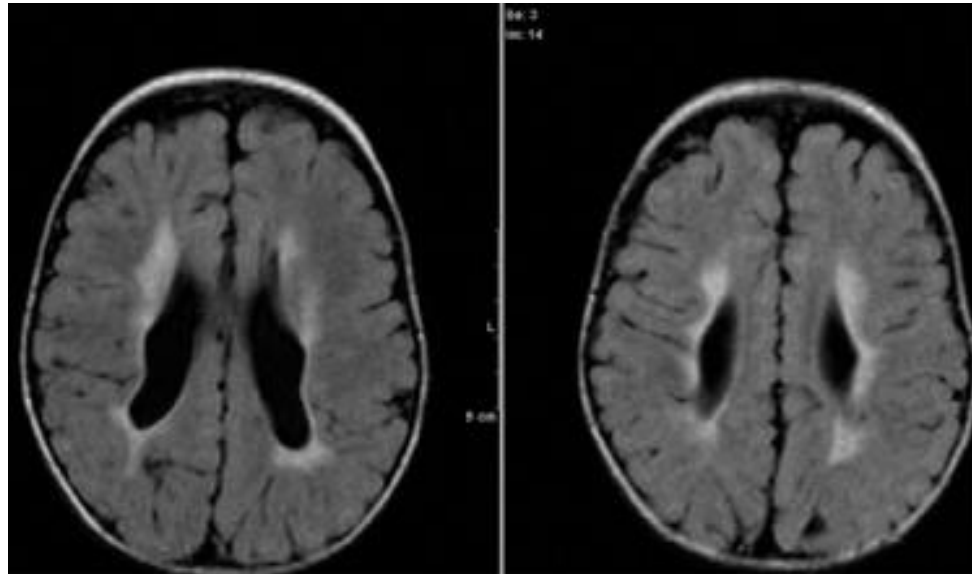
Head Lag

Normal Tone and Strength



PART 2

Central Nervous System Disorders- Cerebral Palsy and Brain Malformations



Cerebral Palsy: The “Central” Diagnosis

- **The most common cause of childhood motor disability:** 1.5–2.5 per 1,000 births; a non-progressive brain injury with a clinical picture that evolves as the child grows.
- **The “Central” pattern:** ↑ tone, ↑ reflexes, clonus, and a Babinski sign — an upper motor neuron pattern
- **Risk factors:** prematurity (<32 weeks), hypoxic-ischemic injury, in utero stroke or infection— though up to 15% have no identified cause.
- **Other developmental delays**
- **Seizures**
- **Don’t wait to refer:** asymmetric hand use before 12 months, persistent toe-walking, or parental concern about development all warrant PT/OT and pediatric neurology referral before a formal diagnosis is made.



Brain Malformations: When Structure Explains the Delay

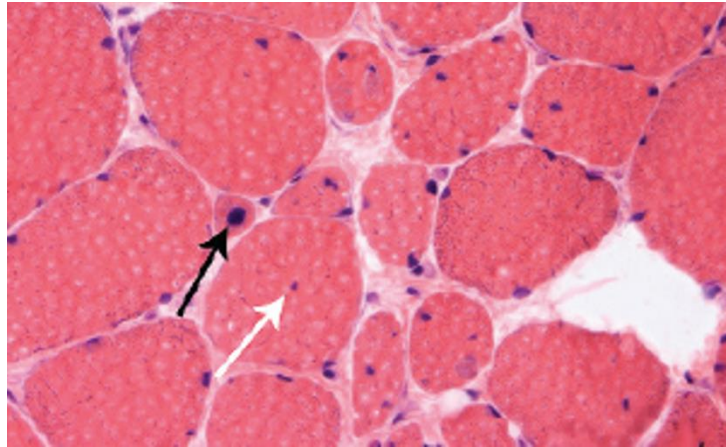
Malformation	Typical Clues
Cortical (lissencephaly, polymicrogyria, schizencephaly)	Seizures, marked global delay, $\pm$ abnormal tone
Posterior fossa (Dandy-Walker, cerebellar hypoplasia)	Macrocephaly, hydrocephalus in infancy, truncal ataxia, incoordination
Chiari malformation type 1	Occipital headache worse with cough/Valsalva, gait ataxia, scoliosis
Corpus callosum agenesis	Variable — seizures, delay, or incidental finding

Consider a brain MRI and neurology referral when: head circumference crosses percentiles (up or down), seizures accompany the motor concern, cognitive/language delay is out of proportion to motor findings, or headache worsens with Valsalva.



PART 3

Neuromuscular Disorders DMD, SMA, Myopathies



Neuromuscular Disorders- Red Flags

- Any regression of motor skills, at any age.
- Gowers sign or calf pseudohypertrophy.
- **An elevated CK** (roughly normal 60–300 IU/L in children) — refer regardless of how mildly elevated.
- **In boys specifically: any developmental delay** — motor, language, or global, not just gait — warrants a CK; DMD can present with speech/cognitive delay before weakness is obvious
- **Ptosis, fatigable weakness, or bulbar symptoms** (dysphagia, nasal voice, weak cry).
- Family history of DMD, SMA, or unexplained neuromuscular death.
- **Any hypotonic, weak infant (“floppy baby”)** — always refer.



Duchenne Muscular Dystrophy: The Basics

- **X-linked recessive;** caused by out-of-frame mutations in the DMD gene → absent dystrophin.
- **Dystrophin** normally stabilizes the muscle cell membrane during contraction; without it, fibers break down with repeated use.
- **Incidence ~1 in 5,000 live male births** — the most common childhood muscular dystrophy.
- **About one-third of cases are de novo mutations** — a negative family history does NOT rule out DMD.
- **DMD is a brain disease too:** dystrophin is also expressed in brain — language delay affects roughly 40–50% of boys, and rates of autism spectrum disorder, ADHD, and intellectual disability are all higher than the general population (Cyrułnik et al., 2007; Vaillend et al., 2025).



Disease Progression

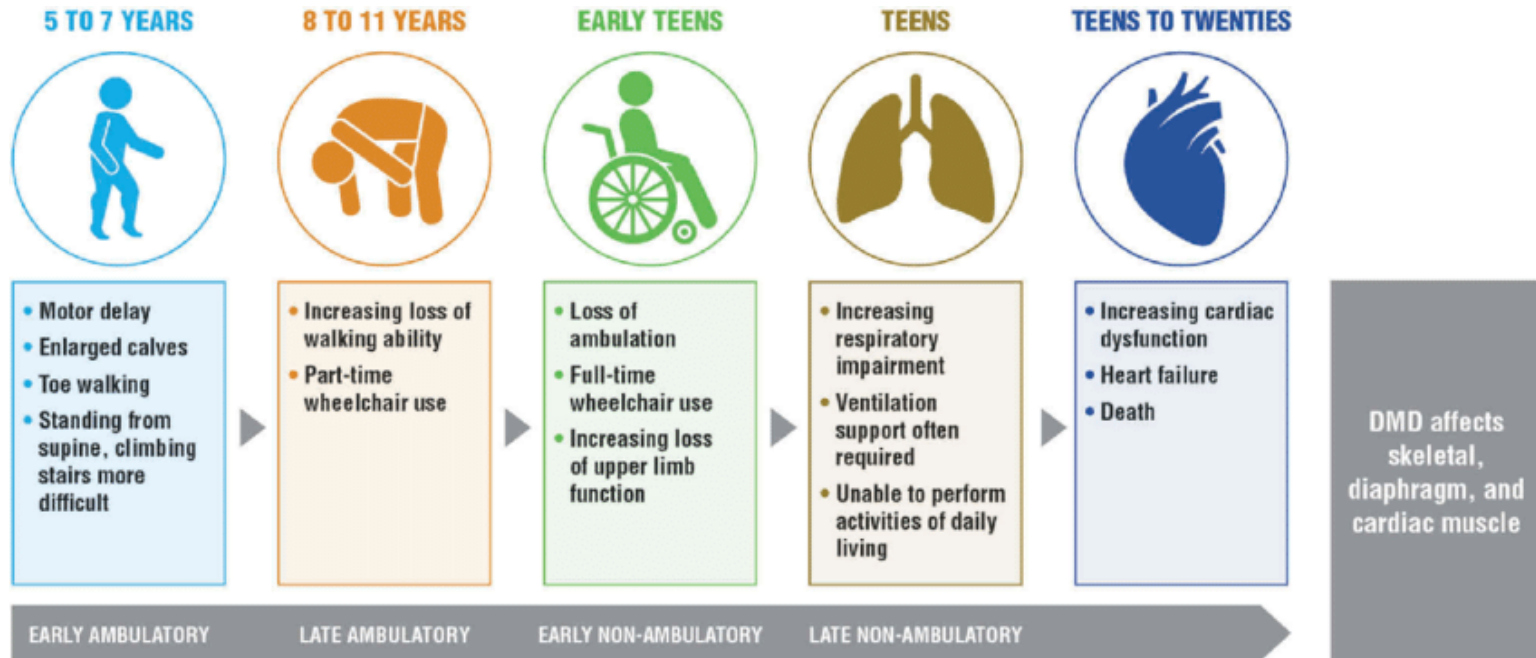


Table II. Percentage of signs and symptoms first reported to care providers by patients with Duchenne dystrophy without family history of dystrophy (n = 111).

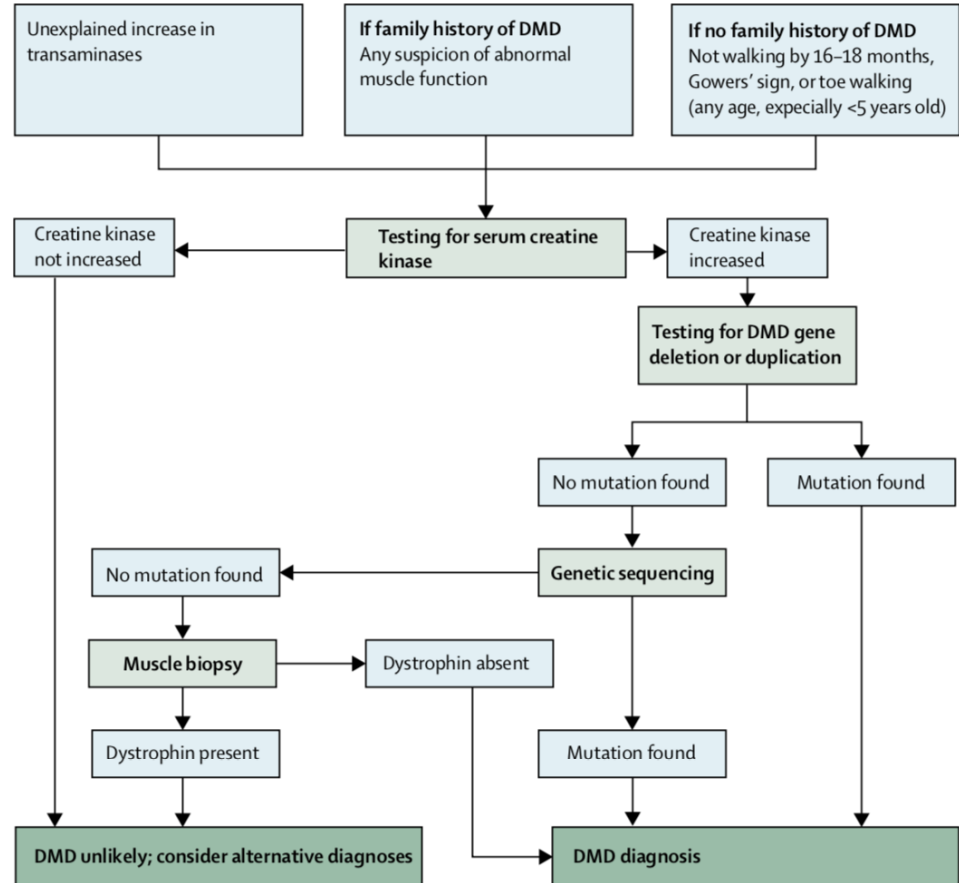
Finding	Age when first signs or symptoms are noted (y)			
	<1.5	≥1.5 and <3	≥3 and <5	≥5
All cases	27.9	29.7	37.8	4.5
Motor or mobility-related				
Abnormal gait	9.7	12.1	11.9	20.0
Frequently falling/clumsy	6.5	15.2	33.3	20.0
Gross motor delay	58.1	48.5	38.1	40.0
Inability to keep up with peers in motor Activities	0	12.1	26.2	80.0
Loss of motor skills	0	0	4.8	0
Muscle hypotonia	16.1	0	7.1	0
Muscle pain	3.2	6.1	11.9	0
Muscle weakness	32.3	6.1	40.5	80.0
Trouble walking	0	6.1	7.1	0
Trouble walking or running	19.4	54.6	38.1	40.0
Trouble climbing	6.5	24.2	31.0	40.0
Trouble rising or getting up	12.9	21.2	23.8	20.0
Nonmotor				
Speech delay or articulation difficulties	9.7	18.2	16.7	20.0
Behavioral issues	0	0	4.8	0
Calf hypertrophy	0	6.1	7.1	0
Cognitive delay	0	0	7.1	0
Failure to thrive/poor weight gain	16.1	0	4.8	0
Other	16.1	9.1	2.4	20.0

The most prevalent SS in each age group are shown in **bold** type.

Diagnosis of DMD

- Elevated CK >10K
- LFT's: high AST,ALT and LDH. Normal GGT
- Muscle biopsy (rare)
- Targeted genetic testing

When to suspect DMD



Management

Medical

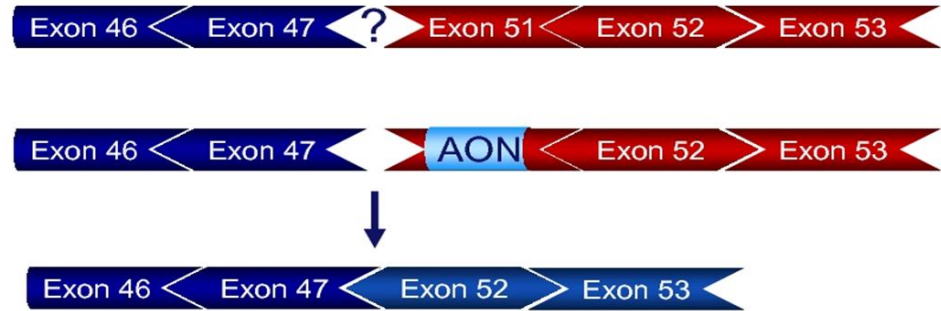
- Steroids
 - Prednisone
 - Deflazacort
 - Vamorolone
- Givinostat
- Exon skipping
- Gene transfer therapy
- Cardiac medications

Non-medical

- Pulmonary surveillance and NIV
- Cardiac surveillance
- Bone health surveillance
- Rehab and therapy support
- Neurobehavioral support'
- Nutritional support

Exon Skippers

- Amondys 45 – Casimersen
- Viltepso 53 – Viltolarsen and Golodirsen
- Exondys 51 – eteplirsen (FDA approved in 2016)



•Excision of exon 51 during pre-mRNA splicing of the dystrophin RNA transcript

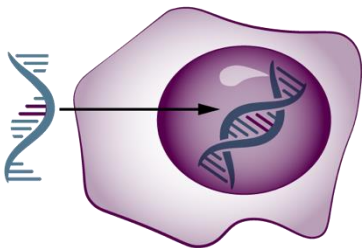
•Out-of-frame mutation → in-frame mutation

•**Converting Duchenne → Becker**

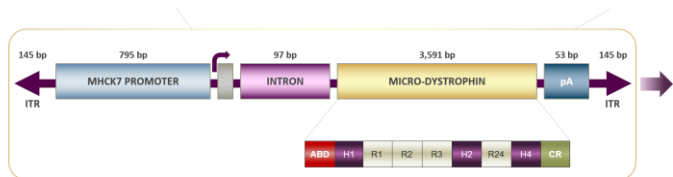
Gene Transfer Therapy- Elevidys

GENE TRANSFER

Adds a new gene



Introduces a new or modified gene into the body to help treat the disease

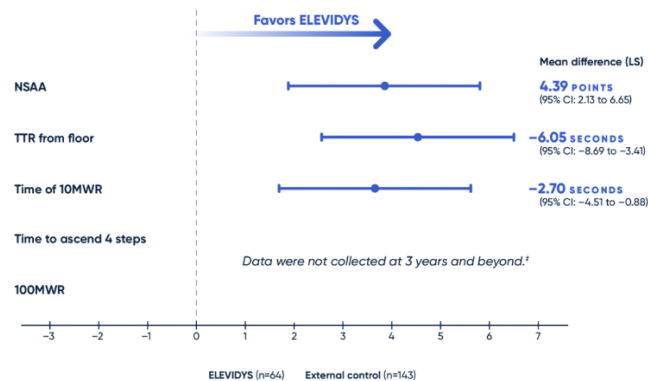


Micro-dystrophin is in clinical trials and has not been FDA reviewed or approved.

3-YEAR RESULTS

ELEVIDYS slowed disease progression²

Prespecified endpoint: Functional outcomes from Study 3 (EMBARK) at 3 years in participants now aged 7 to <11 years; ELEVIDYS vs external control



[†] Results for time to ascend 4 steps and 100MWR remained stable over 2 years; there was no external control comparison available.

Liver	Gastrointestinal	Hematological	Cardiopulmonary	CNS	Other Events
Serious acute liver injury^{1,4,6,7}	- Severe vomiting^{1,8} - Dehydration^{1,8} - GI infection^{4,5} - GI bleed⁶	- Complement mediated HUS^{3,8,11} - Severe thrombocytopenia^{3,4,11}	- Cardio-pulmonary insufficiency² - Elevated troponins⁴	Severe headache^{9,10}	- Death⁶ - Sepsis⁶ - Grade 2 pyrexia⁹ - Severe pain (back, extremities, etc)⁹

Therapeutic Pipeline for DMD by Development Phase (2026)

Each bar represents a treatment / program



*RGX-202 is currently in Phase 2/3 (in Phase 2/3, it is entering phases 2 and 3).

TOTAL:
~29 programs / distinct studies
(Not all programs are included here)



Gene therapy



Exon skipping (new)



Exon skipping (1st generation)



Cell therapy



Anti-inflammatory



Other small molecules

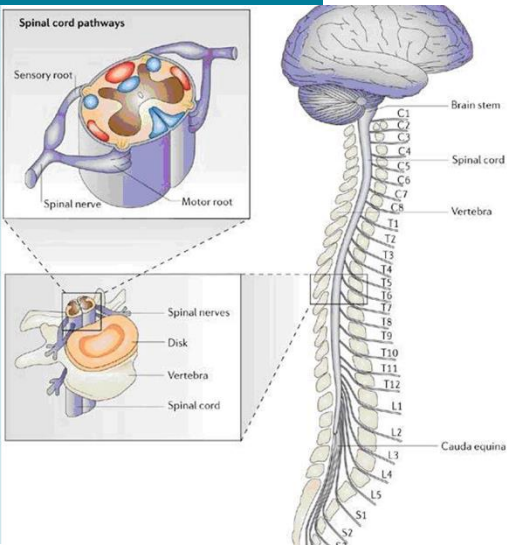
Data updated in May 2026

DMD: What the GP Should Do

- **Order a CK** on any boy with delayed motor OR language/global milestones, frequent falls, Gowers sign, or calf hypertrophy — even without a family history. Language delay can precede obvious weakness in DMD (Cyrułnik et al., 2007; Noritz & Murphy, 2013).
- **Refer to neurology .**
- **Once a diagnosis is confirmed in the family,** screen female relatives who are potential carriers for cardiomyopathy risk and obtain CK for male siblings
- **Start the PT referral early** — don't wait for a confirmed diagnosis if the exam is already concerning.



SMA: The Basics



- Loss of anterior horn cell in the spinal cord and motor nuclei of the brainstem leading to **progressive degeneration of motor neurons and muscle atrophy**
- **Autosomal recessive**; biallelic loss of SMN1
- **SMN2** is a “backup” gene — copy number (usually 2–4) largely determines phenotype severity and is checked at diagnosis.
- **Second most common autosomal recessive disorder after cystic fibrosis**; carrier frequency ~1 in 40–60.
- **Classic phenotypes (Type 0–4)** span prenatal-onset severe to mild adult-onset — but early treatment has dramatically changed this natural history.



Newborn Screening Changed Everything

- **SMA was added to the federal Recommended Uniform Screening Panel in 2018;** all 50 states and DC now screen for it.
- **Washington State:** the Board of Health approved adding SMA in 2019, with screening effective statewide August 1, 2020.
- **Presymptomatic treatment is transformative:** infants treated before symptom onset can achieve normal or near-normal motor milestones.
- **A positive NBS result is an urgent, same-day neuromuscular referral** — every day matters for infants with 2 SMN2 copies.

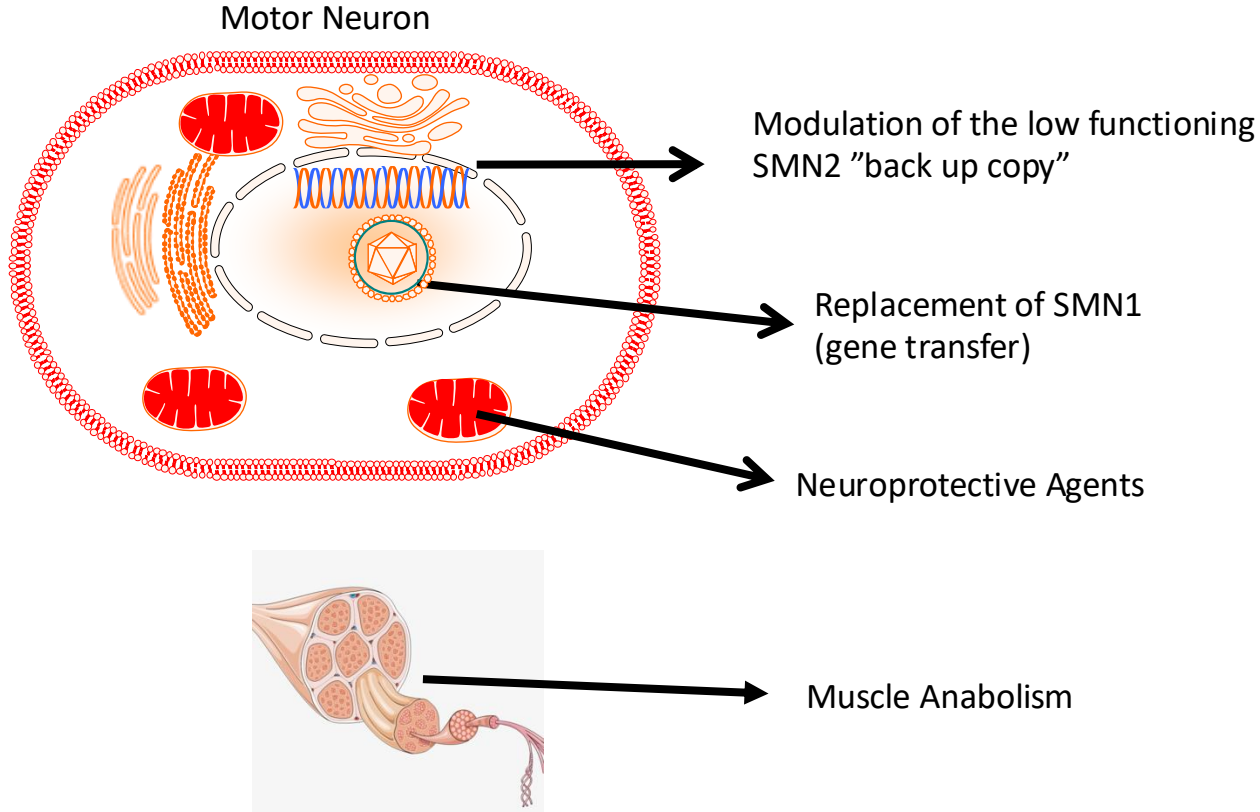


SMA: If It Wasn't Caught at Birth

- **NBS only covers infants born after screening started** — consider SMA in any older child with a compatible picture, or anyone born out of state/country.
- **Type 2 (never walks independently) and Type 3 (walks, may lose ambulation later)** can present later in childhood: proximal weakness, tongue fasciculations, fine hand tremor, hyporeflexia/areflexia.
- **Hallmark pattern:** symmetric proximal > distal weakness, legs weaker than arms, preserved sensation, normal-to-mildly-elevated CK.
- **Cognition is normal** — a helpful distinguishing feature from many congenital myopathy/CMD syndromes.



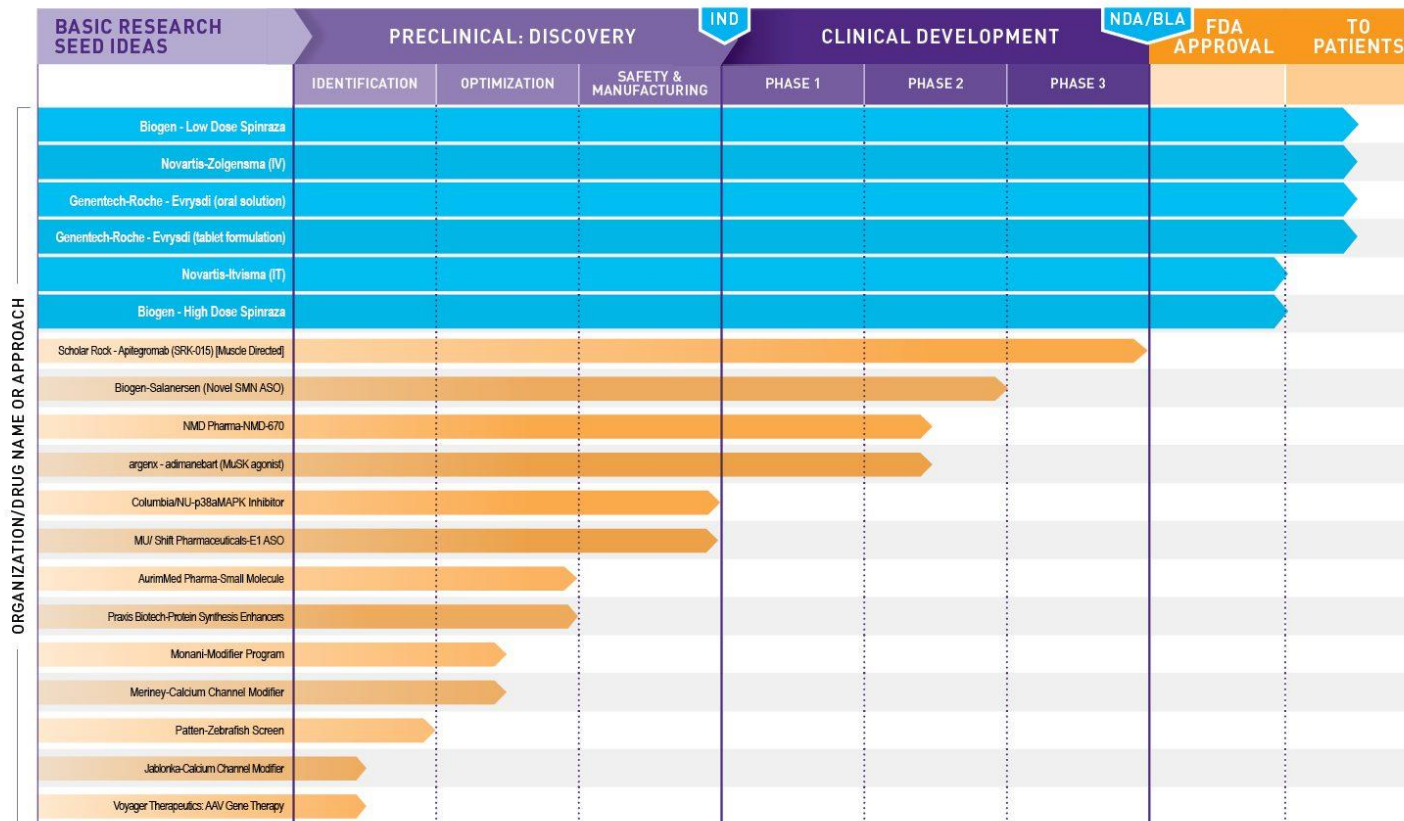
SMA- Therapeutic Approaches





SMA DRUG PIPELINE

We're funding and directing research with more breadth and depth than ever before. We know what we need to do to develop and deliver new therapies, which could also work in combination, to reach our goal of treatments for all ages and types. And we're on the verge of further breakthroughs that will continue to change the course of SMA, and eventually lead to a cure.

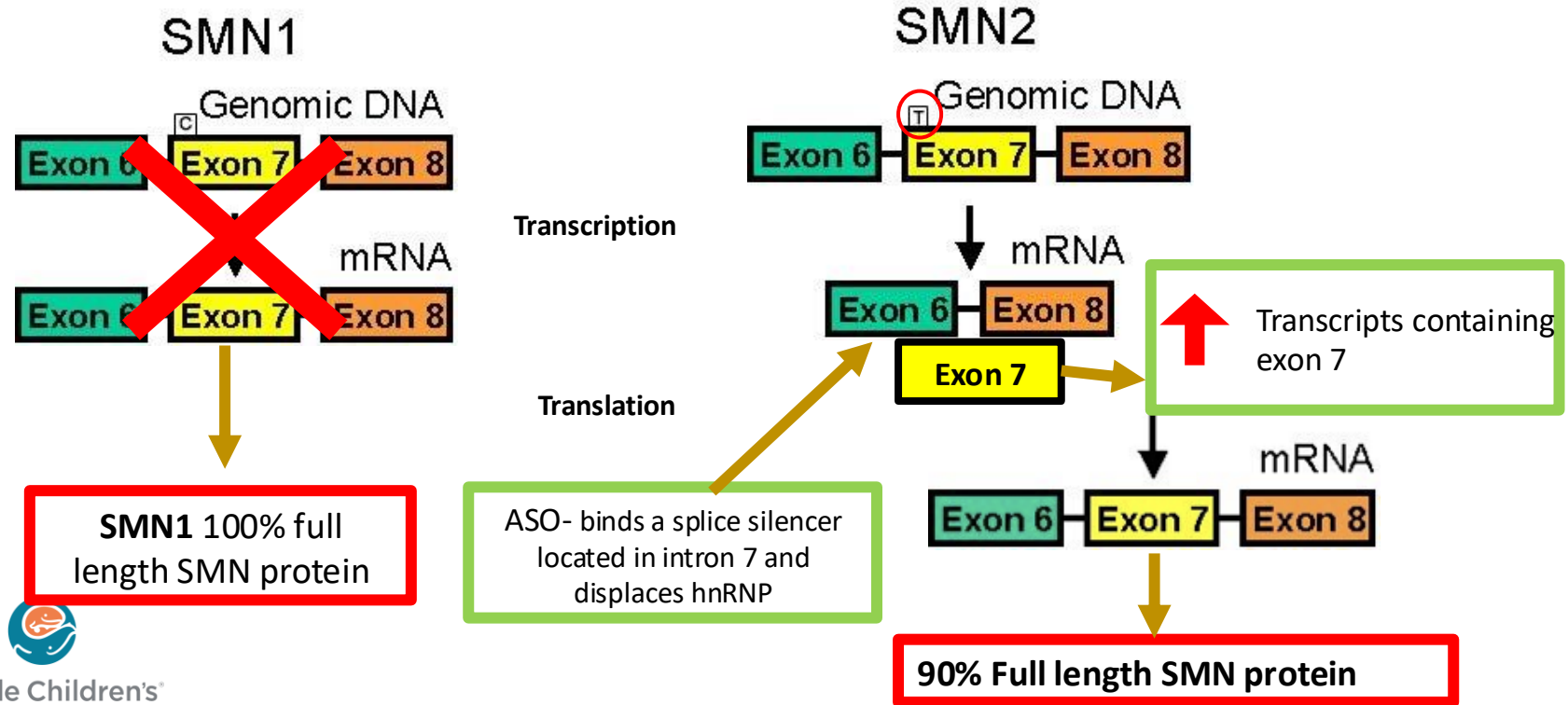


SMA: The Treatment Landscape

Therapy	Mechanism	Route	Notes	FDA approval	Price
Nusinersen (Spinraza™)	ASO boosts SMN2 exon 7 inclusion	Intrathecal For life	Loading doses, then every 4 months indefinitely	December 2016	\$375,000/year
onasemnogene abeparvovec-xioi/brve (Zolgensma™/Itivisma™)	AAV9 gene therapy delivers SMN1	One-time IV or intrathecal infusion	High side effect profile	May 2019/ Nov 2025	\$2.2/2.5 million/dose
Risdiplam (Evrysdi™)	Small-molecule SMN2 splicing modifier	Oral, daily For life	Only oral option; usable across a broad age range	August 2020	\$409,000/year
Apitegromab (Isemyld™)	Myostatin inhibitor	IV, monthly	Only muscle targeted therapy	September 2026	\$310,000/year

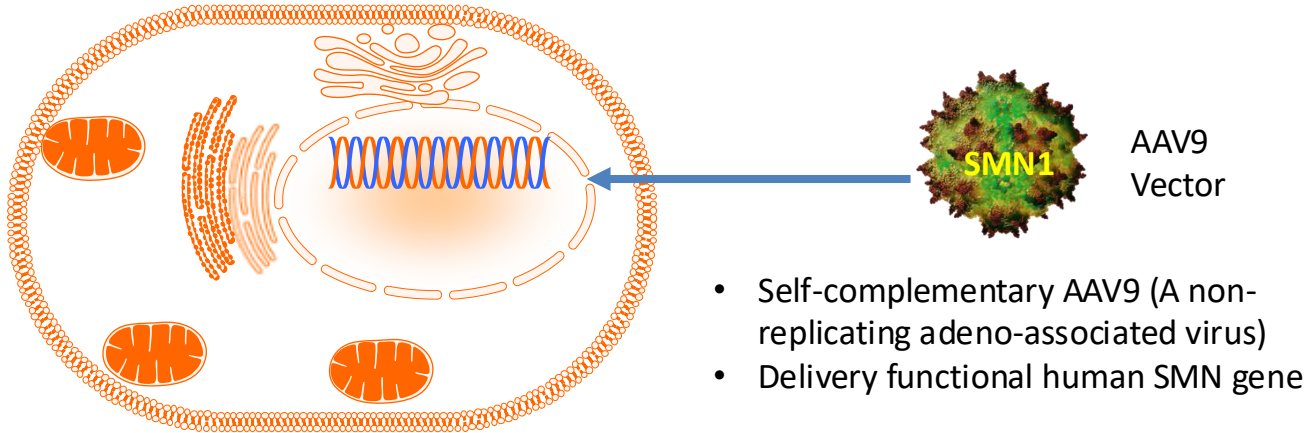


ASO Exon Inclusion



onasemnogene abeparvovec-xioi/brve

Gene Transfer



Apitegromab - Myostatin Inhibitor

Mechanism

- Monoclonal antibody that inhibits **myostatin activation**, promoting muscle growth and strength.
- Targets **muscle**, complementing SMN-directed therapies.

SAPPHIRE Phase 3

- Type 2/3 SMA receiving standard SMN-directed therapy
- **+1.8 points HFMSE** vs placebo at 12 months
- **30.4% vs 12.5%** achieved ≥ 3 -point HFMSE improvement

Key Point

- First FDA-approved **muscle-targeted therapy for SMA**.
- **Combination therapy** to address residual muscle weakness



SMA: What the GP Should Do

- **Confirm every newborn screen result** and verify that they were born in the US and timing of NBS in their state
- **Any hypotonic, weak infant with reduced/absent reflexes** → urgent neurology referral, even with a normal NBS (screening can miss rare SMN1 point mutations).
- **For older children with a compatible pattern (proximal muscle weakness and decreased/absent reflexes)** , urgent referral to neurology; consider sending SMA testing
- Gene transfer therapy has many potential side effects. Communicate with neurologist with any concerns
- In the setting of illness consult the neuromuscular team- management for these kids is different



Congenital Myopathies: When Hypotonia Doesn't Resolve

- **Present from birth/infancy** with hypotonia, weakness, and often a distinctive face: long/thin facies, high-arched palate, ptosis.
- **Course is typically static or very slowly progressive** — unlike DMD, most children do NOT lose previously acquired skills **and actually gain skills**
- **CK is usually normal or mildly elevated** — a key clue that separates myopathy from muscular dystrophy.
- **Historically named for muscle biopsy appearance;** genetic panel testing has now largely replaced biopsy as the first-line test.
- **Management** is supportive



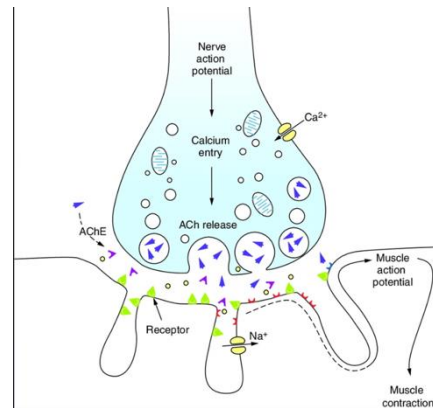
Congenital Myopathies

Subtype	Key Genes	Clinical Pearl
Nemaline myopathy	NEB, ACTA1, others	Watch for cardiopulmonary/respiratory involvement
Central core / multiminiore disease	RYR1	Malignant hyperthermia risk — flag before any general anesthesia
Centronuclear / myotubular myopathy	MTM1 (X-linked, severe), DNM2, BIN1	Prominent ophthalmoplegia/bulbar involvement; X-linked form often severe in infancy
Congenital fiber-type disproportion	ACTA1, TPM2/3, others	Diagnosis of exclusion by biopsy pattern; variable severity



Congenital Myasthenic Syndromes: Fatigable, Antibody-Negative

- **Genetic disorders of neuromuscular junction transmission** — presynaptic, synaptic, or postsynaptic defects
- **Presents in infancy/early childhood** with feeding difficulties, fatigable weakness, ptosis, ophthalmoplegia, worse with activity/late in the day, may improve with rest.
- **Normal cognition and reflexes**
- **Diagnosis: clinical pattern + electrodiagnostic testing + genetic testing**
- **CK is normal**
- **Treatment is gene/mechanism-specific; some therapies can improve symptoms while others may worsen specific CMS subtype**



Four Diagnoses, Side-by-Side

Feature	DMD	SMA	Congenital Myopathy	CMS
Onset	Toddler / preschool	Birth–infancy (or later)	Birth / infancy	Infancy–early childhood
Course	Progressive	Progressive (LMN)	Static / slowly progressive	Static, fatigable
CK	Markedly ↑	Normal / mild ↑	Normal / mild ↑	Normal
Key sign	Gowers, calf hypertrophy	Tongue fasciculations, Weakness: prox>distal	Facial weakness, ptosis, hypotonia	Fatigable ptosis, worse through day
First test	CK + DMD gene panel	SMN1 deletion test	Genetic myopathy panel	Genetic CMS panel

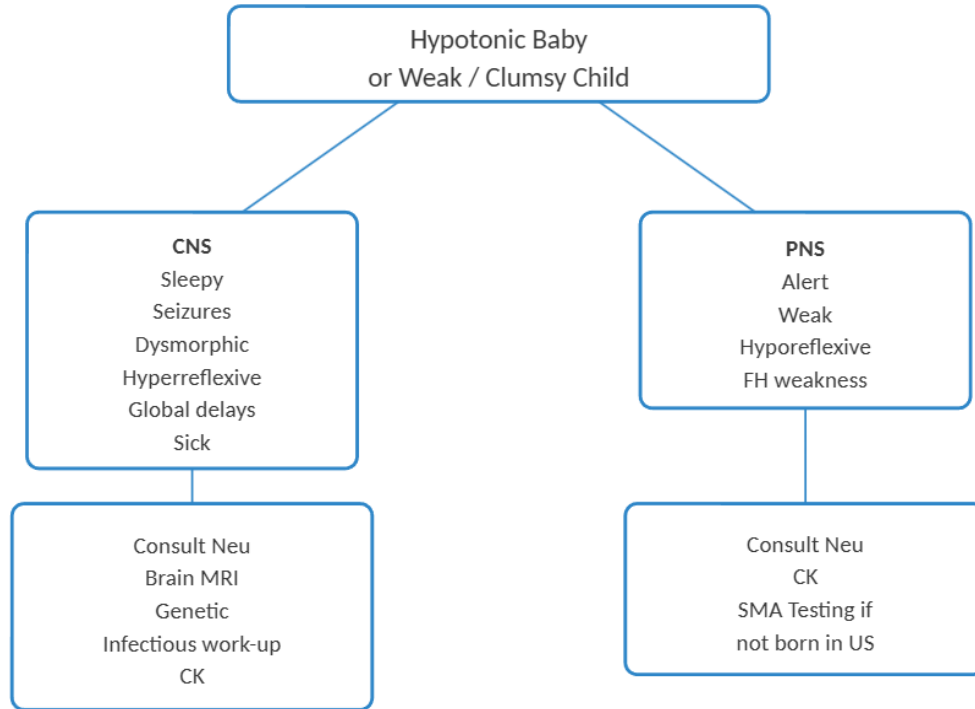


PART 4

Putting It Into Practice: Workup, Referral, and PT



Diagnostic Approach



*** Not sure if a work up is needed?
Consider PT or
neurology referral ***



When to Test, When to Refer, When to Worry

- **Test now (in your office):** CK, basic metabolic panel/electrolytes, TSH — cheap, fast, and often diagnostic or at least narrowing.
- **Refer now (don't wait on labs):** any regression, Gowers sign, calf hypertrophy, ptosis/fatigability, or a floppy infant.
- **Worry most about:** respiratory or bulbar symptoms (weak cry, poor feeding, choking, breathlessness) — these need urgent same-day evaluation, not a routine referral.
- **When in doubt, refer:** a normal neurological exam or PT evaluation reassures a family; a missed diagnosis delays treatment



The Case for Early PT Referral

- **PT evaluation doesn't require a confirmed diagnosis** — refer as soon as a motor concern is identified.
- **Early PT establishes a functional baseline**, screens for contractures, and can pick up subtle patterns (fatigability, compensatory strategies) that support the diagnosis.
- **PT often sees the child most regularly** — a key partner in monitoring functional change over time.



Key Takeaways

- **Most clumsy kids are just clumsy** — but regression, weakness on exam, or a concerning family history should never be dismissed as developmental variation.
- **History and exam point the way**
- **There are treatments available that are life changing and screening and supportive care can affect lifespan and improve quality of life**
- **When red flags are present:** order CK, refer to pediatric neurology, and start PT — in parallel, not in sequence.



Resources & References

- **Cure SMA — Newborn Screening for SMA:** curesma.org/newborn-screening-for-sma
- **Washington State Department of Health — Newborn Screening Program:** doh.wa.gov
- **Muscular Dystrophy Association — Medical Management, DMD:** mda.org
- **Seattle Children's Neurology Program**



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