Background

- · Primary care settings provide early opportunities to spot symptoms, test, and refer patients with suspected NMD to specialists.
- Of >30 NMDs, many share core clinical features that are important to keep in mind when evaluating patients. Early screening
 can be performed during a clinic visit, and a genetic counselor can help navigate testing needs
- · Several NMDs have interventional treatments that change outcomes, especially when initiated early.
- Information in this document highlights key points from an MDA-hosted, CE-accredited webinar with neurologists who have extensive experience managing pediatric muscular dystrophies.

Most Common Pediatric NMDs

Pediatric NMDs are often inherited, but some result from *de novo* genetic mutations. Symptoms may evolve for weeks to years, depending on the NMD.

СМТ	DMD / BMD	Myotonic Dystrophy	LGMD	SMA	Congenital Dystrophies & Myopathies
 1 in 2,500 Childhood to adulthood onset Mutation in several different genes 	 1 in 5,000 male births Onset 2-5 years old Mutation in <i>DMD</i> gene X-linked BMD is mild form 	 1 in 8,000 worldwide Onset at birth or juvenile-onset Mutation in <i>DMPK</i> gene AD inheritance 	 10-20 in 100,000 worldwide Onset >5 years old 28-34 genetically diverse subtypes AD and AR forms 	 1 in 10,000 births per year (incidence) 1-2 in 100,000 (prevalence) Onset usually 6-18 months old Mutation in <i>SMN1</i> gene 	 1-2 in 100,000 Onset at birth Mutation in several different genes

1. Dowling JJ. Am J Med Genet A. 2018 Apr;176(4):804-841. doi: 10.1002/ajmg.a.38418. 2. Rossor AM. Nat Rev Neurol. 2013 Oct;9(10):562-71. doi: 10.1038/nrneurol.2013.179. 3. Wicklund MP. Continuum (Minneap Minn). 2019 Dec;25(6):1599-1618. doi: 10.1212/CON.00000000000809. 4. Ho G. World J Clin Pediatr. 2015 Nov 8;4(4):66-80. doi: 10.5409/wjcp.v4.i4.66.

What to Watch For: Red Flags for Neuromuscular Disease

"Floppy Infants"		
 Hypotonic ('frog-leg') posture Reduced muscle bulk Limb-girdle pattern weakness Truncal weakness Hyporeflexia; areflexia Facial weakness +/- ptosis Neck weakness, dysphagia, hypoventilation Weak extraocular muscles: opthalmoplegia Alert, typically non-encephalopathic H/o fetal akinesia, polyhydramnios 		

Developed with the expertise of Partha Ghosh, MD, of Boston Children's Hospital and Elena Caron, MD, of Le Bonheur Children's Hospital Last Reviewed: September 2023



When to Suspect Neuromuscular Disease: Core Clinical Features

Abnormal muscle function is the defining feature of NMDs.

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- Gross motor delays
- Difficulty keeping up with peers
- Frequent falls
- Toe-walking
- Exertional myalgias/ cramps (particularly affecting calves)
- Family history (inheritance patterns)

Muscle Symptoms: Fixed

- Impaired gait
- Joint contractures
- Pes cavus foot deformity
- Skeletal deformities (scoliosis)
- Muscle weakness
- Respiratory difficulty

Muscle Symptoms: Episodic*

- Rhabdomyolysis
- Fatigable weakness
- Myalgia
- Exercise intolerance

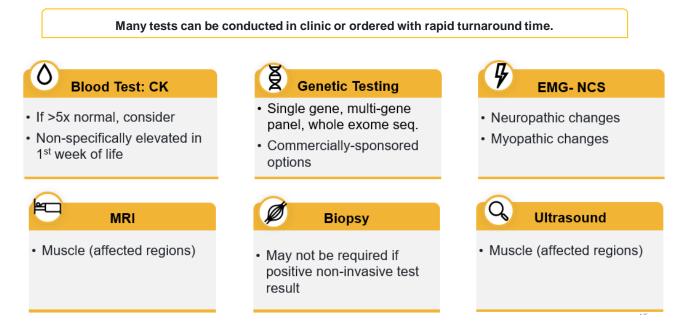
*Intervening exam may be normal

Abnormal Neurological Exam

- Prominent facial weakness +/- ptosis
- Extraocular muscle weakness
- Generalized hypotonic ('frog-leg') posture
- Hyporeflexia
- Weakness/dysfunction of respiratory & bulbar muscles

1. Bonnemann, CG. Neuromuscular Disorders. 2014; 24:289–311. doi: 10.1016/j.nmd.2013.12.011. 2. North, KN. Neuromuscular Disorders. 2014; 24:97–116. doi: 10.1016/j.nmd.2013.11.003.

Suspected Neuromuscular Disease: Core Tests for Workup





Resources to Help Guide Referral

Key Publications

- Bonnemann, CG. Neuromuscular Disorders. 2014; 24:289–311. doi: <u>10.1016/j.nmd.2013.12.011</u>.
- Dowling JJ. Am J Med Genet A. 2018 Apr;176(4):804-841. doi: <u>10.1002/ajmg.a.38418.</u>
- Dubowitz V. Color Atlas of Muscle Disorders in Childhood. 1989. (out-of-print)
- North KN. Neuromuscular Disorders. 2014; 24:97–116. doi: <u>10.1016/j.nmd.2013.11.003.</u>

MDA Medical Education

VIEW WEBINAR: Genetic Testing & Counseling in NMD

- 25 min, hosted by a genetic counselor
- Reviews available genetic tests and how to order
- Companion flashcards available
- <u>https://youtu.be/IYdbyOyPmJA</u>

Helpful Tools to Assess Suspected NMD

- Creatine kinase testing: Checking CK for developmental delay can help rule out muscular dystrophies
- Early referral: Even if CK levels are normal, a NMD specialist can help manage motor delays and muscle weakness.
- Connect with a local MDA Care Center: <u>MDA.org/care/mda-care-centers</u>
- Bookmark ChildMuscleWeakness.org: Algorithms, videos, guide for primary care
- Visit AAP HealthyChildren.org screening tool: <u>healthychildren.org/English/MotorDelay/Pages/default.aspx#</u>



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Access companion CE-accredited MDA webinar here

