Pediatric Neuromuscular Disorders: Red Flags & Testing for Primary Care

A Resource for Clinicians

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.

CMT

- **1 in 2,500**
- Childhood to adulthood onset
- Mutation in several different genes

DMD / BMD

- **1 in 5,000 male births**
- Onset 2-5 years old
- Mutation in *DMD* gene
- X-linked
- BMD is mild form

Myotonic Dystrophy

- **1 in 8,000 worldwide**
- Onset at birth or juvenile-onset
- Mutation in *DMPK* gene
- AD inheritance

LGMD

- **10-20 in 100,000 worldwide**
- Onset >5 years old
- 28-34 genetically diverse subtypes
- AD and AR forms

SMA

- **1 in 10,000** births per year (incidence)
- 1-2 in 100,000 (prevalence)
- Onset usually 6-18 months old
- Mutation in *SMN1* gene

Congenital Dystrophies & Myopathies

- **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.0000000000000809. 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

Hypotonic Children

- Decreased muscle bulk
- Muscle hypertrophy / pseudohypertrophy (DMD)
- Scoliosis
- Foot drop and pes cavus: neuropathy
- Bulbar weakness, impaired swallow or breathing out of proportion to weakness
- Respiratory insufficiency

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

MDA MEDICAL EDUCATION

Pediatric Neuromuscular Disorders: Red Flags and Testing (cont.)

A Resource for Clinicians

When to Suspect Neuromuscular Disease: Core Clinical Features

Abnormal muscle function is the defining feature of NMDs.

Clinical History

- 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

Many tests can be conducted in clinic or ordered with rapid turnaround time.

Blood Test: CK

- If >5x normal, consider
- Non-specifically elevated in 1st week of life

Genetic Testing

- Single gene, multi-gene panel, whole exome seq.
- Commercially-sponsored options

EMG- NCS

- Neuropathic changes
- Myopathic changes

MRI

- Muscle (affected regions)

Biopsy

- May not be required if positive non-invasive test result

Ultrasound

- Muscle (affected regions)

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

MDA MEDICAL EDUCATION

Pediatric Neuromuscular Disorders: Red Flags and Testing (cont.)

A Resource for Clinicians

Resources to Help Guide Referral

Key Publications

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

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
- https://youtu.be/lYdbyOyPmJA

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:** MDA.org/care/mda-care-centers
- **Bookmark** ChildMuscleWeakness.org**:** Algorithms, videos, guide for primary care
- **Visit AAP HealthyChildren.org screening tool**: healthychildren.org/English/MotorDelay/Pages/default.aspx#

Access companion CE-accredited MDA webinar here

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

MDA MEDICAL EDUCATION