Becker Muscular Dystrophy (BMD): Overview & Differentiating Features

A Resource for Clinicians

Background

- Becker muscular dystrophy (BMD) is often treated as a subset of Duchenne muscular dystrophy (DMD).
- There are no clear guidelines for diagnosing/managing BMD; best-practicing sharing can help.
- This document captures highlights from an MDA webinar with a BMD expert.
- View the companion webinar here.

Core Clinical Features

	BMD	DMD
Clinical History	• Onset of muscle weakness after age 10 • Slow progression • Loss of ambulation in the early 20s	• Presents with muscle weakness before age 5 • Affects legs and pelvis and worsens over time • May cause falls and difficulty walking • Wheelchair dependency before age 13
Muscle Symptoms	• Presentation is variable • Phenotype ranges from myalgia with cramping and elevated CK to severe muscle weakness in early childhood	• Progressive symmetric muscle weakness (proximal > distal) with calf hypertrophy • Activity-induced cramping • Flexion contractures of the elbows (late)
Cardiac Symptoms	• Cardiomyopathy usually develops later • Some have severe cardiomyopathy and mild weakness • DCM contribute to 50% of BMD deaths	• Cardiac complications contribute to 20% of deaths
Other Abnormalities	• Cognitive impairment less common	• Cognitive impairment • Fatigue • Loss of balance and coordination • Problems breathing • Muscle weakness in arms, neck and other areas of body

1. Darras BT, et al. GeneReviews® [Internet]. 1993–2024. PMID: 20301298.

Diagnostic Testing

Can we clearly distinguish DMD from BMD?
Clinical history, examination, and supportive tests help guide diagnosis.

Blood Test: CK

- **DMD:** Elevated CK (10-100X)
- **BMD:** Elevated CK (10-100X)

Genetic testing

- **DMD:** Out-of-frame deletions
- **BMD:** In-frame deletions

Muscle Biopsy

- **DMD:** Absent dystrophin immunostaining
- **BMD:** Reduced dystrophin immunostaining

MRI/Ultrasound

- **DMD**: Increase T2 hyperintensity/ echogenicity
- **BMD**: Normal or minimal changes

EMG-NCS

- **DMD:** Diffuse irritable myopathy
- **BMD:** Normal to mild CNE changes

Developed with the expertise of Sumit Verma, MD, Associate Professor of Pediatrics and Neurology, Emory University School of Medicine and Pediatric Neurologist, Children's Healthcare of Atlanta, Atlanta, Georgia.

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Multi-disciplinary Care

There is currently no BMD cure. Management aims to help with symptoms and improve quality of life.

Symptom Management

- Common treatments target muscle weakness, cardiomyopathy, and scoliosis.
- The diversity of symptoms experienced by patients with BMD often necessitates care by:
  - Cardio
  - Pulmonary
  - Orthopedic
  - Speech & Language
  - Physical Therapy & Occupational Therapy (including home modifications or assistive equipment)
  - Nutrition
  - Pain
  - Psychosocial
  - Palliative care

Management of Cardiomyopathy

- Therapeutics:
  - ACE inhibitors and beta-blockers improve survival and clinical status in adults with dilated cardiomyopathy (DCM) and are recommended for children with DCM.
- Transplantation:
  - In a multicenter study, 25% BMD patients underwent cardiac transplantation 5 months after cardiomyopathy diagnosis.

1. Birnkrant et al. Lancet Neurol. 2018 17(3):251-267. 2. Connuck DM. Am Heart J. 2008 Jun;155(6):998-1005. doi: 10.1016/j.ahj.2008.01.018.

Treatments on the Horizon

Corticosteroids (prednisone, deflazacort, vamorolone) are prescribed to decrease muscle inflammation and improve strength for patients with DMD.

Prednisone for BMD

- A 2022 single center open-label study evaluated efficacy of once-weekly prednisone (0.75–1 mg/kg) administered over 24 weeks to patients with LGMD or BMD.
  - Only one patient recruited with BMD, so no safety or efficacy conclusions could be reached.
  - Recruiting patients with BMD can be challenging, despite relatively high prevalence of the disease.

Other Emerging Therapies

- EDG-5506 (Myostatin Inhibitor)
- (+)-epicatechin (Antioxidant)
- Vamorolone (NFkB inhibitor)
- Givinostat (HDAC inhibitor)
- Others (Metformin, Tadalafil)

1. Zelikovich AS. J Neuromuscul Dis. 2022;9(2):275-287. doi: 10.3233/JND-210741.

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Natural History Studies

Natural history studies are helping to define BMD presentation and disease progression.

Italian BMD study (2016):

- Cohort of ages 6-69
- People with X-51 and 48 deletions showed milder or asymptomatic disease
- People with 45-X deletions showed severe weakness and progression
- Results predict better outcomes for exon 51 than 45 skipping in DMD

CINRG BMD study (2024):

- Longitudinal design
- Variable progression of outcomes
- Significant heterogeneity of the clinical phenotype
- Disease progression is largely manifest in adulthood

1. Bello 2016. Open Access; Bello L. Sci Rep. 2016 Sep 1;6:32439. doi: 10.1038/srep32439. 2. Clemens 2024. Open Access; Clemens PR. J Neuromuscul Dis. 2024;11(1):201-212. doi: 10.3233/JND-230178.

Encouraging patients to enroll in registries can help answer outstanding questions in BMD

- **GRASP-01-002:** Defining Endpoints in BMD (Virginia Commonwealth University)
- **Duchenne Registry** (The Duchenne Registry)
- **MOVR (neuroMuscular ObserVational Research) Data Hub** (MDA)

Useful Recommendations

1. Presentation of BMD is unique. Boys presenting with muscle breakdown, rhabdomyolysis, and/or cardiomyopathy should be tested for BMD.

2. Careful interpretation of genetic testing results is imperative. Early diagnosis enables proactive disease management.

3. The natural history of BMD indicates that little change occurs over the first 18 years, but that significant decline can occur later in the course of disease. Close follow-up and monitoring at an MDA Care Center is advised.

4. New therapies are on the horizon for BMD. Widespread participation in patient registry opportunities like MDA's MOVR and ongoing clinical trials will help move new therapies forward and provide hope for improved outcomes.

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BMD: Key Resources

Key Publications

- Verma S. Review of DMD for the pediatricians in the community. Clin Pediatr. 2010 Nov;49(11):1011-7.
- Straub V, Guglieri M. An update on BMD. Curr Opin Neurol. 2023 Oct 1;36(5):450-454.

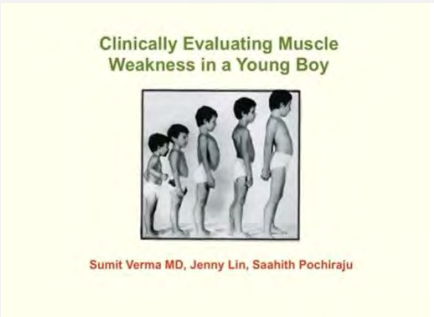
MDA Medical Education

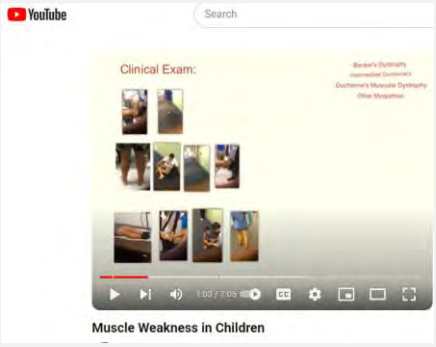
- Genetic Testing & Counseling in NMD
  (25 min webinar with genetic counselor)
- MDA.org/MedEd:
  Sign up for Monthly Report to receive alerts on upcoming events and resources

Helpful Tools & Videos

- Verma, Lin, Pochiraju. Clinically Evaluating Muscle Weakness in a Young Boy

  https://www.youtube.com/watch?v=t5zNunmmKtk&authuser=0





Access companion MDA webinar here

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