

What is Nemaline Myopathy?

Nemaline myopathy (NM) is an inherited neuromuscular disease characterized by muscle weakness and the presence of rod-shaped structures, known as nemaline bodies, in affected muscle fibers.¹ NM involves defects in the organization and function of components of muscle fibers that are involved in muscle contraction. The inability of the muscles to contract properly results in muscle weakness and other symptoms.²

What are the symptoms of Nemaline Myopathy and what treatment is available?

Nemaline myopathy is a disease that varies in severity and age at presentation, even within families. There are congenital (at or near birth), childhood, and adult-onset forms.¹

Congenital NM ranges from mild (also called “typical” NM) to severe. Symptoms of congenital nemaline myopathy include¹:

- Muscle weakness that is most severe in the face, neck, and proximal muscles (those closest to the body) of the arms and legs
- Hypotonia (low muscle tone)
- Absence or weakness of certain body reflexes called deep tendon reflexes
- Feeding problems
- Respiratory problems due to weakness of muscles involved in breathing and coughing
- Difficulty maintaining normal levels of oxygen and carbon dioxide while sleeping
- Recurrent lower respiratory tract infections
- Joint hypermobility (“double jointed”) in infancy and early childhood
- Joint contractures (joint stiffness that prevents full extension) and scoliosis (abnormal curvature of the spine)

“Typical” congenital NM is the most common form of NM and presents soon after birth or within the first year of life. There can be delayed achievement of gross motor milestones, abnormal gait, and speech or swallowing difficulties in a subset of children. It is typically slowly progressive or nonprogressive, and most individuals with this type of NM lead independent, active lives.¹

Severe congenital (neonatal) NM can present prenatally with decreased fetal movement, joint contractures, or excess amniotic fluid; or NM can present at birth. Muscle weakness is profound, and death often occurs within the first year due to breathing problems or pneumonia.¹

The childhood- and adult-onset forms of NM are milder with progressive muscle weakness as the predominant symptom.¹

How is *NEB*-related Nemaline Myopathy inherited?

NM is a disease caused by mutations in at least seven known genes.¹ Nemaline myopathy due to mutations in the *NEB* gene is an autosomal recessive disease.¹ An individual who inherits one copy of a *NEB* gene mutation is a “carrier” and is not expected to have related health problems. An individual who inherits any two mutations in this gene, one from each parent, is expected to be affected with NM.

If both members of a couple are carriers of any mutation in the *NEB* gene, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.



Who is at risk for *NEB*-related Nemaline Myopathy?

NEB-related NM can occur in individuals of all races and ethnicities. A single mutation in the *NEB* gene has been found in the Ashkenazi (Eastern European) Jewish population with a carrier frequency of approximately 1 in 168³ and calculated disease incidence of approximately 1 in 113,000.

Having a relative who is a carrier or is affected can also increase an individual's risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a *NEB* gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results. There are seven genes associated with NM. Inheritest looks for mutations in the most common NM-related gene, *NEB*, but does not assess a person's risk for being a carrier of the other less common NM-related genes.

Where can I get more information?

- Muscular Dystrophy Association (USA): www.mda.org/disease/nm.html
- Muscular Dystrophy Campaign (UK): www.muscular-dystrophy.org/about_muscular_dystrophy/conditions/113_nemaline_myopathy
- Muscular Dystrophy Canada: http://www.muscle.ca/fileadmin/National/Muscular_Dystrophy/Disorders/Nemaline_E.pdf

References

1. North K, Ryan M. Nemaline myopathy. *GeneReviews*. Available at: <http://www.ncbi.nlm.nih.gov/books/NBK1288/>. Accessed March 21, 2012.
2. Genetics Home Reference. *NEB*. Available at: <http://ghr.nlm.nih.gov/gene/NEB>. Accessed: March 31, 2012.
3. Scott SA *et al*. Experience with carrier screening and prenatal diagnosis for 16 Ashkenazi Jewish genetics diseases. *Hum Mutat*. 2010 Nov; 31(11): 1240-1250.

