

What are Niemann-Pick Disease Types A and B?

Niemann-Pick disease types A (NPD-A) and B (NPD-B) are autosomal recessive diseases characterized by enlarged liver and spleen, progressive lung disease, and failure to gain weight and grow as expected. Niemann-Pick type A also leads to progressive loss of intellectual and motor skills.¹ The signs and symptoms of NPD-A and NPD-B result from the inability of the body to break down properly a lipid known as sphingomyelin, which accumulates in various organs in the body.¹ Niemann-Pick disease types A and B are also known as acid sphingomyelinase deficiency and belong to a group of diseases called lysosomal storage disorders.² This group includes Niemann-Pick disease type C, which is genetically and clinically distinct.

What are the symptoms of Niemann-Pick Disease Types A and B and what treatment is available?

The symptoms of Niemann-Pick disease type A (NPD-A) are typically noted in the first few months of life and include:^{1,3}

- Enlarged liver and spleen that worsens over time
- A cherry-red spot of the macula of the retina
- Lung disease and frequent respiratory infections
- Hypotonia (low muscle tone)
- Difficulties feeding and sleeping
- Loss of ability to roll over, sit with support, babble, or smile responsively as the disease progresses
- Death typically by three years of age

Although considerable variability exists in expression, symptoms of Niemann-Pick disease type B are milder than type A, have later onset, and include:¹

- Enlarged spleen ranging from mild to severe
- Gradual decline in lung function
- Cholesterol and triglycerides levels in the abnormal range
- Short stature and low weight
- Intellectual disability and psychiatric disorders in a subset of patients
- Survival into adulthood for most

There is currently no cure for Niemann-Pick disease types A and B, and treatment is supportive of symptoms.¹ Newborn screening for Niemann-Pick disease is available in some states.⁴

How are Niemann-Pick Types A and B inherited?

Niemann-Pick types A and B are autosomal recessive diseases caused by mutations in the *SMPD1* gene.¹ An individual who inherits one *SMPD1* mutation is a “carrier” and is not expected to have related health problems. An individual who inherits two *SMPD1* mutations, one from each parent, is expected to be affected with Niemann-Pick type A or B depending on the combination of mutations.

If both members of a couple are carriers, 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 Niemann-Pick Types A and B?

Niemann-Pick Types A and B can occur in individuals of any ethnic background. Niemann-Pick disease type A is prevalent in individuals of Ashkenazi (Eastern European) Jewish ancestry. Among Ashkenazi Jews, the carrier frequency is estimated to be 1 in 116, and the incidence is calculated to be approximately 1 in 53,800.⁵ While accurate estimates of disease incidence are not available for Niemann-Pick disease type B, it is most common in individuals of Turkish, Arabian, and North African ancestry.⁶

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 gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

- National Institute of Neurological Disorders and Stroke: <http://www.ninds.nih.gov/disorders/niemann/niemann.htm>
- National Niemann-Pick Disease Foundation: <http://www.nnpdf.org/>
- Gene Reviews: <http://www.ncbi.nlm.nih.gov/books/NBK1370/>

References

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5. Scott SA, et al. Experience with Carrier Screening and Prenatal Diagnosis for 16 Ashkenazi Jewish Genetic Disorders. 2010 *Hum Mutat* 31:1240-1250.
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