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Niemann-Pick disease types A and B

What is Niemann-Pick disease, types A and B?

Niemann-Pick disease, type A or B, is 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 Niemann-Pick types A and B result from the inability of the body to properly break down a lipid known as sphingomyelin, which accumulates in various organs in the body.[1] Niemann-Pick disease, type A or B, is also known as acid sphingomyelinase deficiency and belongs 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]

- Enlargement of 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, symptoms of Niemann-Pick disease type B are milder than those of type A, have later onset, and may 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
- Survival into adulthood for most patients

There is currently no cure for Niemann-Pick disease, type A or B, and treatment is supportive.[1] Newborn screening for Niemann-Pick disease is available in some states.[4]

How is Niemann-Pick disease, types A and B, inherited?

Niemann-Pick disease, type A or B, is an autosomal recessive disease 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 disease type A or B.

If both members of a couple are carriers of a mutation in the same gene, the risk of having 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 disease, types A and B?

Niemann-Pick disease types A and B can occur in individuals of any ethnic background with a carrier frequency of 1 in 250.[5] 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.[6] 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.[7]

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/

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