

What is Niemann-Pick disease, type C?

Niemann-Pick disease, type C, is an inherited disease characterized by an inability of the body to properly move cholesterol and lipids within cells. Symptoms of Niemann-Pick disease, type C, are caused by the accumulation of cholesterol and lipids, primarily in the liver and brain. Niemann-Pick disease, type C, belongs to a group of diseases called lysosomal storage disorders.¹ This group also includes Niemann-Pick disease, types A and B, which are genetically and clinically distinct from Niemann-Pick disease, type C.

What are the symptoms of Niemann-Pick disease, type C and what treatment is available?

The symptoms of Niemann-Pick disease, type C, vary and are dependent on the age of onset. Prenatally, fetal ultrasound may detect abnormal fluid accumulation in one or more areas of the body. Newborns may have symptoms of liver disease, pulmonary disease, or hypotonia (decreased muscle tone). Most individuals are diagnosed in childhood with symptoms including:²

- Enlarged liver or spleen, or jaundice
- Clumsiness
- Movement disorders
- Inability to move eyes vertically
- Progressive speech deterioration
- Developmental delay
- Seizures
- Difficulties with sleeping and eating

Adult-onset Niemann-Pick disease, type C, has a slower progression and is associated with dementia or psychiatric symptoms. The lifespan of individuals with Niemann-Pick disease, type C, varies from a few days to over 60 years, with most individuals surviving to the second or third decade of life. There is no cure for Niemann-Pick disease, type C, at this time. Treatment focuses on managing symptoms and preventing secondary complications.³

How is Niemann-Pick disease, type C, inherited?

Niemann-Pick disease, type C, is an autosomal recessive disease that is caused by mutations in two different genes. Mutations in the *NPC1* gene account for the majority of cases of Niemann-Pick disease, type C. Mutations in the *NPC2* gene are responsible for the remaining cases.³

An individual who has only one mutation in either of these genes is a carrier and is not expected to have related health problems. An individual who inherits two mutations in the same gene, one from each parent, is expected to be affected with Niemann-Pick disease, type C. For example, a child with two *NPC1* mutations is expected to be affected, but a child with one *NPC1* mutation and one *NPC2* mutation is a carrier.

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, type C?

Niemann-Pick disease, type C, can occur in individuals of all races and ethnicities, with an incidence of approximately 1 in 120,000 live births.² Among families with Niemann-Pick disease, type C, approximately 90% have *NPC1* mutations and approximately 4% have *NPC2* mutations.³ Therefore, the carrier frequency for *NPC1* is calculated to be 1 in 183, and the carrier frequency for *NPC2* is calculated to be 1 in 866.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics 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?

Niemann-Pick UK: <http://www.niemann-pick.org.uk/niemann-pick-disease/niemann-pick-type-c>

National Niemann-Pick Foundation: <http://www.nnpdf.org/>

References

1. Millat, G *et al.* Niemann-Pick C1 Disease: The I1061T Substitution Is a Frequent Mutant Allele in Patients of Western European Descent and Correlates with a Classic Juvenile Phenotype. *Am. J. Hum. Genet.* 1999; 65: 1321-1329
2. Vanier MT. Niemann-Pick disease type C. *Orphanet Journal of Rare Diseases*. Available at <http://www.ajrd.com/content/5/1/16>. Accessed: January 4, 2012.
3. Patterson M. Niemann-Pick disease type C. *Gene Reviews*. Available at <http://www.ncbi.nlm.nih.gov/books/NBK1296/>. Accessed: December 29, 2011.