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CARRIER SCREEN

What is Niemann-Pick Disease Type C?

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

What are the Symptoms of Niemann-Pick Disease Type C and What Treatment is Available?

The symptoms of NPC 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 present with 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 NPC has a slower progression and is associated with dementia or psychiatric symptoms. The lifespan of individuals with NPC 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 NPC at this time. Treatment focuses on managing symptoms and preventing secondary complications[3].

How is Niemann-Pick Disease Type C Inherited?

NPC 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 NPC. 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 NPC. For example, a child with two *NPC1* mutations would be expected to be affected, but a childwith one *NPC1* mutation and one *NPC2* mutation would be only a carrier.

If both members of a couple are carriers of a mutation in the same 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 Niemann-Pick Disease Type C?

NPC can occur in individuals of all races and ethnicities, with an incidence of approximately 1 in 120,000 live births[2]. Among families with NPC, 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?

- NIH Office of Rare Diseases Research - Genetic and Rare Diseases (GARD) Information Center www.rarediseases.info.nih.gov/GARD/
- National Niemann-Pick Foundation http://www.nnpdf.org/

References

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