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CARRIER SCREEN

What are the Neuronal Ceroid-Lipofuscinoses?
The neuronal ceroid-lipofuscinoses (NCLs) are a group of inherited diseases characterized by deterioration of intellectual and motor abilities, seizures, vision loss, and decreased life expectancy.[1] They involve defects in a variety of enzymes responsible for breaking down or moving substances, called lipofuscins, within cells. Symptoms associated with the NCLs are due to a toxic build-up of lipofuscins in the cells and tissues of the body, particularly in the brain.[2] Some of the more common names for forms of this disease include Batten disease, Santavuori-Haltia disease, and Jansky-Bielschowsky disease.[1]

What are the symptoms of the Neuronal Ceroid-Lipofuscinoses and what treatment is available?
The NCLs are a group of related diseases that vary in severity and age at presentation. The NCLs are categorized based on age of onset, symptoms, and findings noted on skin biopsy. All forms of NCLs cause seizures and loss of mental and motor function.[1] Additional symptoms vary depending on type and may include:

Select Forms of NCL[1]

Type	Most Common Causative Gene	Age of Onset	Symptoms May Include	Typical Life Expectancy
Infantile (Santavuori-Haltia disease)	*PPT1*	about 6-24 months (may be earlier)	• Seizures • Loss of mental and motor function • Progressive vision loss • Small head size	2-9 years
Late-Infantile (Jansky-Bielschowsky disease)	*TPP1*	about 2-4 years	• Seizures • Loss of mental and motor function • Progressive vision loss	6 years-adolescence (may be longer)
Late-Infantile, Finnish variant	*CLN5*	about 4-7 years	• Seizures • Loss of mental and motor function • Progressive vision loss	13-35 years
Juvenile (Batten disease, Spielmeyer-Vogt disease)	*CLN3*	about 4-8 years	• Seizures • Loss of mental and motor function • Progressive vision loss	Late teens to early 20s, some into 30s

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			• Behavior problems • Speech problems • Sleep problems	
Northern Epilepsy	*CLN8*	about 2-10 years	• Seizures • Loss of mental and motor function • Rarely, vision loss	Possibly beyond 60 years
Adult (Kuf's disease)	Rarely, *PPT1*	Variable, but typically about 30 years	• Seizures • Loss of mental and motor function • Behavior problems	About 10 years after onset

There is no cure for any of the NCLs. Treatment involves supportive care for symptoms and may include nutrition management, medications to control seizures and psychiatric/behavior problems, and physical, occupational, and speech therapies.[1]

How are the Neuronal Ceroid-Lipofuscinoses inherited?
The NCLs are a group of diseases that may be inherited in an autosomal recessive or autosomal dominant pattern that can be caused by mutations in several different genes. The Inheritest Carrier Screen includes mutations in the *PPT1* (also known as *CLN1*), *TPP1* (also known as *CLN2*), *CLN3, CLN5*, and *CLN8* genes, which cause the majority of autosomal recessive NCL.[3]

In an autosomal recessive form of NCL, an individual who inherits one copy of a disease-causing mutation in one of these genes is a "carrier" and does not usually have related health problems. An individual who inherits two disease-causing mutations in the same gene, one from each parent, is expected to be affected with an NCL. For example, a child with two *PPT1* mutations would have an NCL, but a child with one *PPT1* mutation and one *CLN3* mutation would only be a carrier.

If both members of a couple are carriers of an autosomal recessive form of NCL 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 the Neuronal Ceroid-Lipofuscinoses?
The NCLs can occur in individuals of all races and ethnicities, with some types occurring more commonly in individuals of Finnish ancestry.

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Carrier Frequencies by Gene:

Population	Genes	Carrier Frequency[3,4,5]
Finnish	*PPT1* *CLN5* *CLN8*	1 in 70 1 in 115 1 in 135
General	*PPT1* *TPP1* *CLN3*	1 in 480 1 in 250 1 in 230

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?

- Batten Disease Support and Research Association: www.bdsra.org
- Hide and Seek Foundation: For Lysosomal Disease Research: http://www.hideandseek.org/Diseases.html

References

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3. Wisniewski K et al. Neruonal Ceroid Lipofuscinoses: Classification and Diagnosis Advances in Genetics, vol 45 Academic Press 2001
4. Savukoski M et al. *CLN5*, a novel gene encoding a putative transmembrane protein mutated in Finnish variant late infantile neuronal ceroid lipfuscinosis. *Nat Genet* 1998;19: 286-288.
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