

What is neuronal ceroid-lipofuscinosis?

The neuronal ceroid-lipofuscinoses are a group of inherited diseases characterized by deterioration of intellectual and motor abilities, seizures, progressive vision loss, and decreased life expectancy.¹ Individuals with neuronal ceroid-lipofuscinosis have defects in one of several different enzymes responsible for breaking down or moving substances, called lipofuscins, within cells. Symptoms associated with neuronal ceroid-lipofuscinosis 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 neuronal ceroid-lipofuscinosis and what treatment is available?

Neuronal ceroid-lipofuscinosis varies in severity and age at onset. Different forms of the disease may be described based on causative gene, age of onset, symptoms, and findings noted on skin biopsy. All forms of neuronal ceroid-lipofuscinosis cause seizures and loss of mental and motor function.¹ Additional symptoms vary.

Comparison of select forms of neuronal ceroid-lipofuscinosis¹

Neuronal ceroid-lipofuscinosis form	Most common causative gene	Age at onset	Additional symptoms may include	Typical life expectancy
Infantile (Santavuori-Haltia disease)	<i>PPT1</i>	About 6-24 months, or earlier	Progressive vision loss Small head size	2 to 9 years
Late-Infantile (Jansky-Bielschowsky disease)	<i>TPP1</i>	About 2-4 years	Progressive vision loss	6 years – adolescence, or longer
Late-Infantile, Finnish variant	<i>CLN5</i>	About 4-7 years	Progressive vision loss	13 to 35 years
Juvenile (Batten disease, Spielmeyer-Vogt disease)	<i>CLN3</i>	About 4-8 years	Progressive vision loss Behavioral problems Speech problems Sleep problems	Late teens to early 20s, or some into 30s
Northern Epilepsy	<i>CLN8</i>	About 2-10 years	Vision loss	Possibly beyond 60 years
Adult (Kuf's disease)	Rarely, <i>PPT1</i>	Variable, but typically about 30 years	Behavioral problems	About 10 years after onset

There is no cure for any of the neuronal ceroid-lipofuscinoses. 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 is neuronal ceroid-lipofuscinosis inherited?

Neuronal ceroid-lipofuscinosis is caused by mutations in at least 13 different genes.¹ Five of the genes, *PPT1* (also known as *CLN1*), *TPP1* (also known as *CLN2*), *CLN3*, *CLN5*, and *CLN8*, cause the majority of autosomal recessive forms of the disease.^{1,3}

In the autosomal recessive form of neuronal ceroid-lipofuscinosis, an individual who inherits one copy of a disease-causing mutation 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 affected with neuronal ceroid-lipofuscinosis. For example, a child with two *PPT1* mutations is affected, and a child with one *PPT1* mutation and one *CLN3* mutation is a carrier.

If both members of a couple are carriers of mutations 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 neuronal ceroid-lipofuscinosis?

Neuronal ceroid-lipofuscinosis can occur in individuals of all races and ethnicities. Neuronal ceroid-lipofuscinosis mutations in some genes occur more commonly in individuals of Finnish ancestry.

Carrier frequencies by gene:

Population	Genes	Carrier frequency ³⁻⁶
Finnish	<i>PPT1</i>	1 in 67
	<i>CLN5</i>	1 in 115
	<i>CLN8</i>	1 in 135
General	<i>PPT1</i>	1 in 480
	<i>TPP1</i>	1 in 250
	<i>CLN3</i>	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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4. Vesa, J, *et al.* Mutations in the palmitoyl protein thioesterase gene causing infantile neuronal ceroid lipofuscinosis. *Nature* 1995; 376(17):584-587.
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