

What is Sandhoff disease?

Sandhoff disease is an inherited disorder characterized by the progressive degeneration of nerve cells in the brain and spinal cord. Individuals with Sandhoff disease have defects in the enzymes beta-hexosaminidase A and B, which are responsible for breaking down a fatty substance called GM2 ganglioside in the body. Without this enzyme, GM2 ganglioside accumulates, primarily in the brain and nerve cells, causing severe damage.¹

What are the symptoms of Sandhoff disease and what treatment is available?

Symptoms of Sandhoff disease are progressive and vary in severity and age at diagnosis. The infantile form is most common.

Symptoms of infantile-onset Sandhoff disease are typically seen by three to six months of age and may include:^{1,2}

- Spasticity (abnormally tight muscles)
- Reduced attentiveness
- Loss of motor skills, such as crawling or walking
- Cherry-red spot seen upon ophthalmologic (eye) examination
- Blindness
- Seizures
- Enlarged organs (spleen and liver)
- Death usually by early childhood

Symptoms of juvenile-onset Sandhoff disease are typically seen between ages 1.5 and 10 years and may include:³

- Coordination problems or clumsiness, including difficulty walking
- Progressive speech problems
- Intellectual impairment
- Gastrointestinal problems (diarrhea or constipation)
- Muscle wasting (cramps and weakness)
- Seizures
- Visual problems
- Death usually by 4 to 26 years of age (earlier onset is associated with earlier age of death)

Symptoms of adult/late-onset Sandhoff disease are typically seen in adolescence or adulthood, and may include:^{1,4}

- Progressive muscle weakness, often leading to wheelchair use
- Clumsiness and gait disturbances
- Speech and swallowing difficulties
- Urinary incontinence
- Psychosis

There is no cure for Sandhoff disease. Treatment includes supportive care for symptoms, such as medications to control seizures and nutritional and respiratory support.²

How is Sandhoff disease inherited?

Sandhoff disease is an autosomal recessive condition caused by mutations in the *HEXB* gene.¹ An individual who inherits one copy of a *HEXB* gene mutation is a carrier and is not expected to have related health problems. An individual who inherits two *HEXB* mutations, one from each parent, is expected to be affected with Sandhoff disease.

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 Sandhoff disease?

Sandhoff disease can occur in individuals of all races and ethnicities. The incidence is approximately 1 in 422,000,⁵ with a calculated carrier frequency of 1 in 325. It may be found more commonly among select populations such as the Metis Indians in Saskatchewan, Canada, the Lebanese population, and the Creole population of northern Argentina.¹

Having a relative who is a carrier or who is affected can increase an individual's risk of being 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?

March of Dimes: <http://www.marchofdimes.org/complications/tay-sachs-and-sandhoff-diseases.aspx>

National Organization for Rare Disorders (NORD): <http://rarediseases.org/rare-diseases/sandhoff-disease/>

National Tay-Sachs and Allied Diseases Association: www.ntsad.org

References

1. Sandhoff disease. *Genetics Home Reference*. Available at: <http://ghr.nlm.nih.gov/condition/sandhoff-disease>. Accessed September 22, 2016.
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4. Delnooz, CCS *et al*. New cases of adult-onset Sandhoff disease with a cerebellar or lower motor neuron phenotype. *J Neurol Neurosurg Psychiatry*. 2010; 81:968-972.
5. Meikle P *et al*. Prevalence of lysosomal storage disorders. *JAMA*. 1999; 281(3):249-254.