What is Sandhoff Disease?
Sandhoff disease is an inherited disorder characterized by the progressive degeneration of nerve cells in the brain and spinal cord. It involves 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 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.

Infantile-onset Sandhoff disease typically presents by three to six months of age, and symptoms may include1,2:
- 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 four years of age

Juvenile-onset Sandhoff disease typically presents between ages 1.5 to 10 years, and symptoms may include3:
- 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 age 4-26 years (earlier diagnosis tends to lead to earlier age of death)

Adult/Late-onset Sandhoff disease typically presents in adolescence or adulthood, and symptoms may include1,4:
- Progressive muscle weakness, wheelchair use common
- 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 disease caused by mutations in the \textit{HEXB} gene.\textsuperscript{1} An individual who inherits one copy of a \textit{HEXB} gene mutation is a “carrier” and is not expected to have related health problems. An individual who inherits two mutations in the \textit{HEXB} gene, one from each parent, is expected to be affected with Sandhoff disease.

If both members of a couple are carriers, 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\textsuperscript{5}, with a calculated carrier frequency of 1 in 325.

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?
- National Institutes of Health: Office of Rare Diseases Research: \url{http://rarediseases.info.nih.gov/GARD}
- National Tay-Sachs and Allied Diseases: \url{www.ntsad.org}
- Madisons Foundation: \url{www.madisonsfoundation.org}

References