

Tay-Sachs disease

Description

Tay-Sachs disease is a rare, inherited disorder that is characterized by neurological problems caused by the death of nerve cells (neurons) in the brain and spinal cord (central nervous system).

The most common form of Tay-Sachs disease, known as infantile Tay-Sachs disease, becomes apparent early in life. Infants with this disorder typically develop normally until they are 3 to 6 months old. During this time, their development slows and muscles used for movement weaken. Affected infants stop achieving normal developmental milestones and begin to lose previously acquired skills such as turning over, sitting, and crawling. Infants with this condition develop an exaggerated startle reaction to loud noises. As the disease progresses, children with Tay-Sachs disease experience involuntary muscle twitches (myoclonic jerks), seizures, difficulty swallowing (dysphagia), vision and hearing loss, and intellectual disability. An eye abnormality called a cherry-red spot, which is identified by eye examination, is characteristic of this disorder. Children with infantile Tay-Sachs disease usually live only into early childhood.

Two other forms of Tay-Sachs disease, known as juvenile and late-onset, are rare. Signs and symptoms of the juvenile form can appear between the ages of 5 years and late adolescence. Features of late-onset Tay-Sachs disease typically appear in adulthood. People with either of these forms of the condition usually have milder and more variable signs and symptoms than those with the infantile form. Characteristic features of juvenile or late-onset Tay-Sachs disease include muscle weakness, loss of muscle coordination (ataxia), speech problems, and psychiatric symptoms. These signs and symptoms vary widely among people with late-onset forms of Tay-Sachs disease.

Frequency

Tay-Sachs disease is very rare in the general population. The genetic variants (also known as mutations) that cause this disease are more frequently found in people of Ashkenazi (eastern and central European) Jewish heritage than in those with other backgrounds. However, increased education and genetic testing efforts in these at-risk communities have reduced the incidence of this condition in those populations.

The variants responsible for this disease are also more common in certain French-Canadian communities of Quebec, the Old Order Amish community in Pennsylvania, and the Cajun population of Louisiana.

Causes

Variants in the *HEXA* gene cause Tay-Sachs disease. The *HEXA* gene provides instructions for making one part (the alpha subunit) of an enzyme called beta-hexosaminidase A. Beta-hexosaminidase A is located in lysosomes, which are structures in cells that break down toxic substances and act as recycling centers. Within lysosomes, beta-hexosaminidase A helps break down a fatty substance called GM2 ganglioside found in cell membranes.

HEXA gene variants affect the ability of the beta-hexosaminidase A enzyme to break down GM2 ganglioside. As a result, GM2 ganglioside accumulates to toxic levels, particularly in neurons in the central nervous system. Damage caused by the buildup of GM2 ganglioside leads to the dysfunction and eventual death of these neurons, which causes the signs and symptoms of Tay-Sachs disease.

HEXA gene variants that eliminate or severely reduce beta-hexosaminidase A enzyme function likely lead to the infantile form of Tay-Sachs disease, and variants that allow some residual enzyme activity tend to cause the juvenile or late-onset form of the condition.

Because Tay-Sachs disease impairs the function of a lysosomal enzyme and involves the buildup of GM2 ganglioside, this condition is sometimes referred to as a lysosomal storage disorder or a GM2-gangliosidosis.

[Learn more about the gene associated with Tay-Sachs disease](#)

- *HEXA*

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have variants. The parents of an individual with an autosomal recessive condition each carry one copy of the altered gene, but they do not show signs and symptoms of the condition.

Other Names for This Condition

- B variant GM2 gangliosidosis
- GM2 gangliosidosis, type 1
- HexA deficiency
- Hexosaminidase A deficiency
- Hexosaminidase alpha-subunit deficiency (variant B)
- Sphingolipidosis, Tay-Sachs
- TSD

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Tay-Sachs disease (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0039373/>)

Genetic and Rare Diseases Information Center

- Tay-Sachs disease (<https://rarediseases.info.nih.gov/diseases/7737/index>)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Tay-Sachs disease%22](https://clinicaltrials.gov/search?cond=%22Tay-Sachs+disease%22))

Catalog of Genes and Diseases from OMIM

- TAY-SACHS DISEASE; TSD (<https://omim.org/entry/272800>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28Tay-Sachs+Disease%5BMAJR%5D%29+AND+%28Tay-Sachs+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D>)

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