Tay-Sachs Disease

"Genomics and Medicine"

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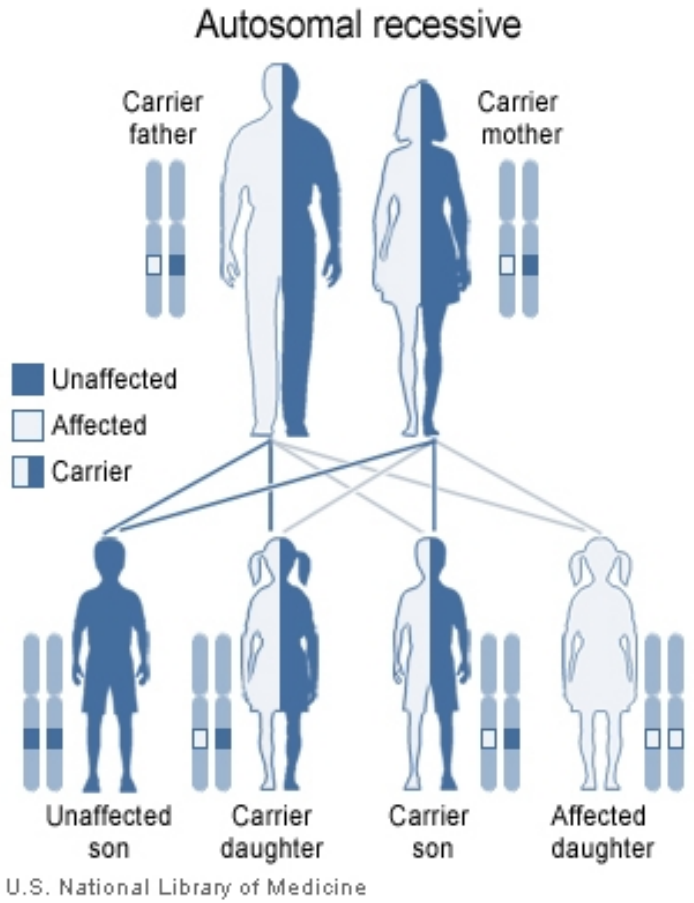
About Tay-Sachs

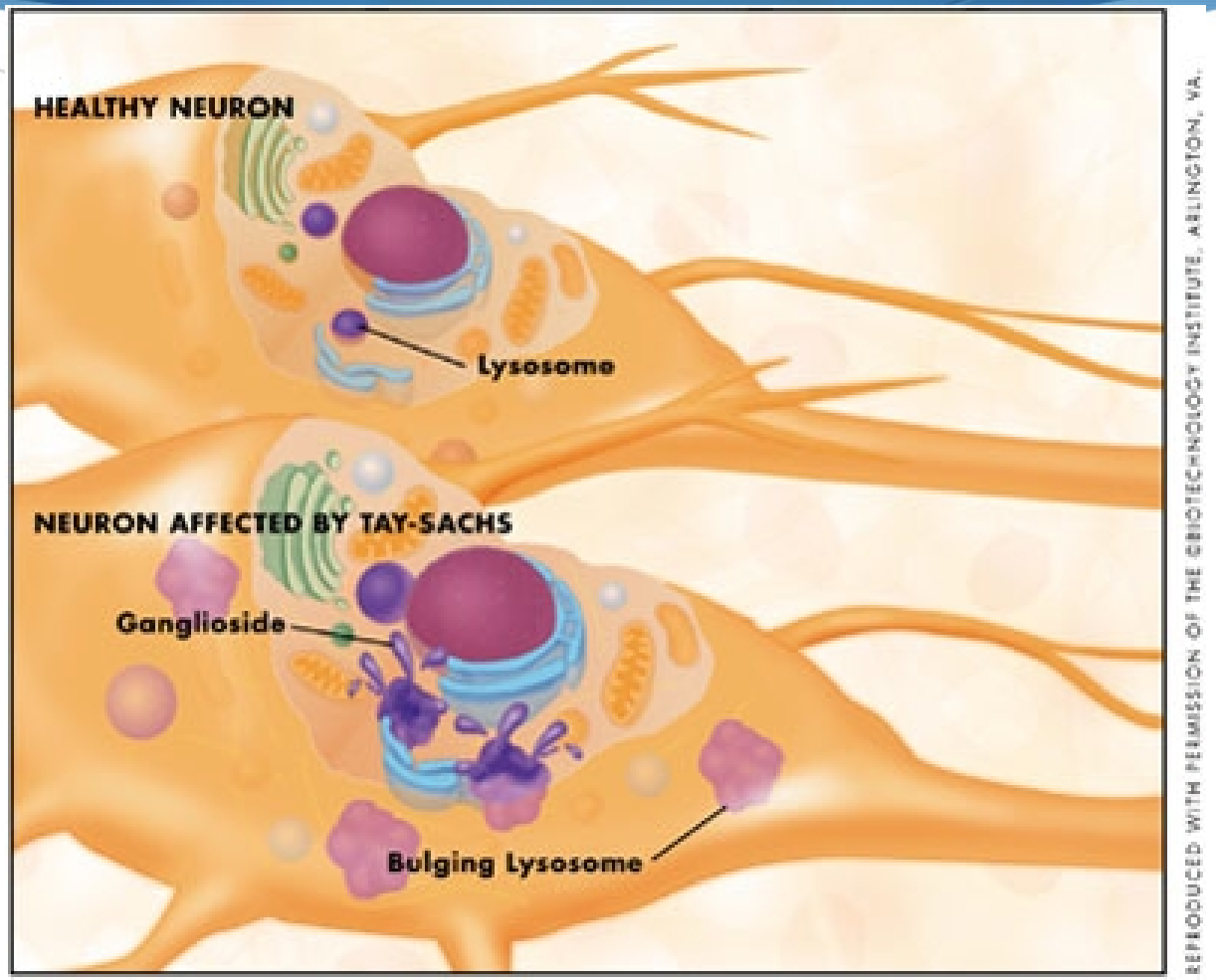
- Autosomal, recessive
- Progressive neurodegenerative disorder
- In the most severe cases, it's fatal by age 2 or 3
- Caused by a mutation in both alleles of a gene on chromosome 15



The Tay-Sachs Gene

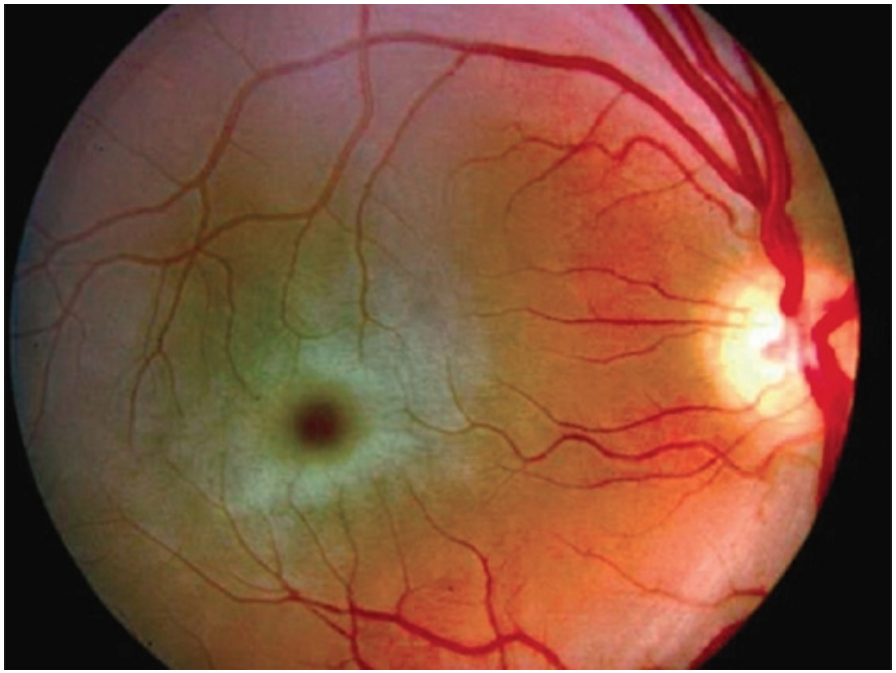
- This gene codes for an enzyme found in lysosomes, an organelle in eukaryotic cells that breaks down large molecules into its components that can be recycled by the cell
- This specific enzyme in the lysosome is absent or at extremely low, inefficient levels in Tay-Sachs individuals
  - Leads to an accumulation of gangliosides, a lipid in neurons
- The progression of Tay-Sachs is directly related to the amount of accumulation of gangliosides

Lipid Accumulation



Diagnosing Tay-Sachs

- Characterized by developmental retardation in infants
- Followed by paralysis, dementia, blindness, and eventually death
- “Cherry-red” spot surrounded by a gray-white area
- Blood test to detect a deficiency in the lysosomal enzyme



Progress Being Made

- Since the causative gene is known, prenatal screening was established in the 1970s
  - Targeted towards Ashkenazi Jews because it's most prevalent among them
  - Has led to a 90% reduction of Tay-Sachs

Treatment Tactics

1. Prevent or slow the production of gangliosides
   - Reduce them to a level that the deficient enzymes can handle
   - Studies inconclusive, still ongoing

1. Normal genes are delivered to the brain to increase the breakdown of gangliosides
   - Delayed the onset of the disease
   - Decreased inflammation of neurons
   - Improved function
   - Extended their life

Late Onset Tay-Sachs

- Unfortunately, there are no treatments for late onset Tay-Sachs.
- Ganglioside synthesis inhibitor shows promise
  - The effectiveness is limited in infants because it's unknown how much irreversible damage occurs before birth.