



Alpers-Huttenlocher syndrome

Alpers-Huttenlocher syndrome is one of the most severe of a group of conditions called the *POLG*-related disorders. The conditions in this group feature a range of similar signs and symptoms involving muscle-, nerve-, and brain-related functions. Alpers-Huttenlocher syndrome typically becomes apparent in children between ages 2 and 4. People with this condition usually have three characteristic features: recurrent seizures that do not improve with treatment (intractable epilepsy), loss of mental and movement abilities (psychomotor regression), and liver disease.

People with Alpers-Huttenlocher syndrome usually have additional signs and symptoms. Most have problems with coordination and balance (ataxia) and disturbances in nerve function (neuropathy). Neuropathy can lead to abnormal or absent reflexes (areflexia). In addition, affected individuals may develop weak muscle tone (hypotonia) that worsens until they lose the ability to control their muscles and movement. Some people with Alpers-Huttenlocher syndrome lose the ability to walk, sit, or feed themselves. Other movement-related symptoms in affected individuals can include involuntary muscle twitches (myoclonus), uncontrollable movements of the limbs (choreoathetosis), or a pattern of movement abnormalities known as parkinsonism.

Affected individuals may have other brain-related signs and symptoms. Migraine headaches, often with visual sensations or auras, are common. Additionally, people with this condition may have decreased brain function that is demonstrated as sleepiness, inability to concentrate, irritability, or loss of language skills or memory. Some people with the condition may lose their eyesight or hearing. People with Alpers-Huttenlocher syndrome can survive from a few months to more than 10 years after the condition first appears.

Frequency

The prevalence of Alpers-Huttenlocher syndrome is approximately 1 in 100,000 individuals.

Causes

Alpers-Huttenlocher syndrome is caused by mutations in the *POLG* gene. This gene provides instructions for making one part, the alpha subunit, of a protein called polymerase gamma (pol γ). Pol γ functions in mitochondria, which are structures within cells that use oxygen to convert the energy from food into a form cells can use. Mitochondria each contain a small amount of DNA, known as mitochondrial DNA (mtDNA), which is essential for the normal function of these structures. Pol γ "reads"

sequences of mtDNA and uses them as templates to produce new copies of mtDNA in a process called DNA replication.

Most *POLG* gene mutations change single protein building blocks (amino acids) in the alpha subunit of pol γ . These changes result in a mutated pol γ that has a reduced ability to replicate DNA. Although the mechanism is unknown, mutations in the *POLG* gene often result in a reduced number of copies of mtDNA (mtDNA depletion), particularly in muscle, brain, and liver cells. MtDNA depletion causes a decrease in cellular energy, which could account for the signs and symptoms of Alpers-Huttenlocher syndrome.

A mutation in the *POLG* gene has not been identified in approximately 13 percent of people diagnosed with Alpers-Huttenlocher syndrome. Researchers are working to identify other genes that may be responsible for the condition.

Inheritance Pattern

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

Other Names for This Condition

- Alpers diffuse degeneration of cerebral gray matter with hepatic cirrhosis
- Alpers disease
- Alpers progressive infantile poliodystrophy
- Alpers syndrome
- diffuse cerebral sclerosis of Schilder
- progressive sclerosing poliodystrophy

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
[/primer/testing/genetic-testing](#)
- Genetic Testing Registry: Progressive sclerosing poliodystrophy
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0205710/>

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Alpers-Huttenlocher+syndrome%22+OR+%22Diffuse+Cerebral+Sclerosis+of+Schilder%22+OR+%22POLG%22>

Other Diagnosis and Management Resources

- GeneReview: POLG-Related Disorders
<https://www.ncbi.nlm.nih.gov/books/NBK26471>
- United Mitochondrial Disease Foundation: Getting a Diagnosis
<http://www.umdff.org/what-is-mitochondrial-disease/getting-a-diagnosis/>

Additional Information & Resources

Health Information from MedlinePlus

- Health Topic: Balance Problems
<https://medlineplus.gov/balanceproblems.html>
- Health Topic: Degenerative Nerve Diseases
<https://medlineplus.gov/degenerativenervediseases.html>
- Health Topic: Genetic Brain Disorders
<https://medlineplus.gov/geneticbraindisorders.html>
- Health Topic: Liver Diseases
<https://medlineplus.gov/liverdiseases.html>
- Health Topic: Movement Disorders
<https://medlineplus.gov/movementdisorders.html>
- Health Topic: Seizures
<https://medlineplus.gov/seizures.html>

Genetic and Rare Diseases Information Center

- Alpers syndrome
<https://rarediseases.info.nih.gov/diseases/5783/alpers-syndrome>

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Alpers Disease
<https://www.ninds.nih.gov/Disorders/All-Disorders/Alpers-Disease-Information-Page>
- National Institute of Neurological Disorders and Stroke: Myoclonus
<https://www.ninds.nih.gov/Disorders/All-Disorders/Myoclonus-Information-Page>
- National Institutes of Health Rare Diseases Clinical Research Network: North American Mitochondrial Disease Consortium
<https://www.rarediseasesnetwork.org/cms/NAMDC>

Educational Resources

- Mayo Clinic: Mitochondrial Disease Biobank
<https://www.mayo.edu/research/centers-programs/mitochondrial-disease-biobank/overview>
- MitoAction
<http://www.mitoaction.org/>
- Orphanet: Alpers-Huttenlocher syndrome
https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=726

Patient Support and Advocacy Resources

- American Liver Foundation: The Progression of Liver Disease
<https://liverfoundation.org/for-patients/about-the-liver/the-progression-of-liver-disease/>
- Muscular Dystrophy Association: Facts About Mitochondrial Myopathies
https://www.mda.org/sites/default/files/publications/Facts_MITO_P-216.pdf
- National Organization for Rare Disorders (NORD): Alpers Disease
<https://rarediseases.org/rare-diseases/alters-disease/>
- United Mitochondrial Disease Foundation: Mitochondrial Disease
<http://www.umdf.org/what-is-mitochondrial-disease/>

Clinical Information from GeneReviews

- POLG-Related Disorders
<https://www.ncbi.nlm.nih.gov/books/NBK26471>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28Alpers-Huttenlocher+syndrome%5BTIAB%5D%29+OR+%28Alpers+syndrome%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- MITOCHONDRIAL DNA DEPLETION SYNDROME 4A (ALPERS TYPE)
<http://omim.org/entry/203700>

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Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3046768/>

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<https://ghr.nlm.nih.gov/condition/alters-huttenlocher-syndrome>

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