

Alpers Disease

Alpers Diffuse Degeneration of Cerebral Gray Matter with Hepatic Cirrhosis, Alpers Progressive Infantile Poliiodystrophy, Diffuse Cerebral Degeneration in Infancy, Poliiodystrophia Cerebri Progressiva, Progressive Cerebral Poliiodystrophy

Alpers disease is a rare mitochondrial condition where the protein that helps replicate and repair the mitochondrial DNA does not work as well as it should. Mitochondria are parts of a cell that help turn the energy we get from food into energy that the body can use. They are also important in the communication between body parts and in creating other materials the body needs.

Cause and Genetics

Alpers disease is considered to have “multifactorial” causes which means it can be caused by many things. These causes can include genetic changes, metabolic factors (or differences in how someone breaks down food), prion-like molecules (proteins that can fold incorrectly and cause damage to the brain), and mitochondrial factors (or changes in part of the cell called the mitochondria).

The most common genetic cause of Alpers disease are changes to the gene *POLG*. People usually have two copies of the *POLG* gene, one inherited from each parent. Alpers disease occurs when there are changes in both copies of the *POLG* gene, also known as autosomal recessive inheritance. Someone who has a change in only one copy of the *POLG* gene is called a carrier, and they usually do not have any medical symptoms. If both parents are carriers, there is a one in four chance with each pregnancy that the child will have Alpers disease. Both males and females can have Alpers disease.

Frequency

Alpers disease is thought to affect approximately 1 in 51,000 to 1 in 100,000 people worldwide. Some genetic changes in *POLG* are present in more people in certain countries, such as Norway, so the frequency can vary depending on ethnicity.

Signs and Symptoms

Alpers disease causes a range of signs and symptoms. These may differ greatly, even among members of the same family, so always check with your provider if new symptoms appear or you are concerned. There is a cluster of three symptoms that make Alpers disease different from other mitochondrial disorders. These include cognitive decline and dementia (which can include trouble with memory, slower thinking skills, loss of awareness and judgment), seizures (abnormal electrical activity in the brain), and liver disease.

Most individuals with Alpers disease do not show symptoms at birth and develop normally for weeks to years before they start to show symptoms. Around 80% of individuals develop symptoms in the first two years of life. The first symptoms seen are usually nonspecific, meaning something that doesn't point to one specific cause. These may include seizures, stiffening of the legs and arms, involuntary jerking of the muscles, and blood sugar issues that signal the first signs of liver disease. In about 25% of cases, babies will have a loss of vision from damage to a specific part of the eye called the cortex. Gastrointestinal problems (problems in the stomach or intestines) and an enlarged heart (cardiomyopathy) may occur. Dementia, also called a cognitive decline, may come, and go, and is often associated with an infection. Seizures may be difficult to control even with medication, and frequent seizures can cause loss of milestones.

There are additional disorders that can appear like Alpers disease but do not have liver disease. These “Alpers-like” disorders are caused by different genetic changes and have a different clinical course.

Diagnosis

Traditionally, Alpers disease can be diagnosed by:

- Measuring biochemical markers in blood, urine, and cerebrospinal fluid (the fluid surrounding the brain and spinal cord)
- Brain studies and imaging looking for changes in the structure of the brain or seizure activity (MRI, MRS, EEG)
- Heart studies looking for structural differences and/or rhythm changes (Echocardiogram, EKG)
- Careful physical examination and growth measurements
- Performing a genetic test to look for changes in genes known to cause Alpers disease

Alpers disease is not included on newborn screening panels. If there is a known family history of Alpers disease, or if parents are known carriers, prenatal testing can be performed on amniotic fluid (the fluid surrounding a baby) or chorionic villi (a specific part of the placenta).

Treatment and Management

Before beginning any treatment or therapy, please consult with your physician.

As of 2022, there is currently no FDA-approved therapy for Alpers disease or known treatment that can cure the root cause of Alpers disease. Treatment and management of Alpers disease are symptomatic (meaning based on the symptoms someone currently has) and supportive. This may include:

- Medication
- Physical therapy to help relieve muscle tightness (spasticity) and maintain or increase muscle tone
- Nutritional support
- Respiratory support
- Traditional treatment of liver features and transplant if needed
- Avoidance of medicines that can be harmful to the liver if possible

Doctors may prescribe medications to try and reduce the number of seizures someone experiences. However, the seizures in Alpers disease sometimes do not respond well to therapy, even at high doses. Therefore, the benefit of seizure control should be weighed against what could be excessive sedation from the medication. There are certain medications, such as a type of seizure medication called sodium valproate, that people with Alpers disease should not use because they can increase the risk of liver failure.

It is important that all those living with or caring for someone with Alpers disease have an emergency protocol letter. These letters, which are written and signed by a doctor, share details about prescribed treatment during a crisis and in emergency room settings.

Clinical Trials

For specific details on clinical trials visit www.mitoaction.org/clinicaltrials or www.clinicaltrials.gov.

Resources

- [Alpers Disease - National Institute of Neurological Disorders and Stroke](#)
- [Alpers Disease - NORD \(National Organization for Rare Disorders\)](#)

Connecting with others who are impacted by a rare disease allows for important information to be shared about day-to-day life, prevents isolation, and gives hope. Please contact MitoAction for peer support opportunities at 888-MITO-411 or email mito411@mitoaction.org.

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