# ALEXANDER DISEASE (AxD)

## What is AxD?

AxD is **a rare, genetic, progressive neurological disorder** that is often severely debilitating and ultimately fatal.[1]

AxD is a type of **leukodystrophy** – a group of rare genetic disorders characterized by the abnormal development of white matter in the central nervous system (CNS), impairing how nerve signals are transmitted between the brain and body.[2]

The condition is estimated to occur in **approximately 1 per 1 to 3 million people worldwide**, accounting for roughly 2% to 12% of all leukodystrophy cases.[2-6]

AxD can **occur at any age and impacts people of all races, ethnicities and regions** of the world.[2,3]

The median length of survival ranges from **14 to 25 years**, depending on age of onset and severity of disease, with later onset generally associated with longer survival.*[7,8]

People diagnosed with AxD typically experience disease progression over several months to years, **but the course of disease can be variable and unpredictable.**[2]

**These data are based upon small samples, and the disease course is seen as variable and unpredictable across all age groups.*

## What causes AxD?

**AxD is primarily associated with pathogenic variants (genetic changes that cause disease) in the glial fibrillary acidic protein (*GFAP*) gene, causing toxic over-production of the protein.[2]**

GFAP is responsible for regulating the shape and interactions of astrocytes, cells that support numerous important functions within the CNS.[2]

The accumulation of GFAP impairs the function of astrocytes, leading to abnormal white matter, neuron dysfunction and degeneration within the CNS.[2]

**Research is currently underway to learn more about the cause and impact of AxD.[3]**

Changes in *GFAP* typically happen randomly *(de novo)* and are not inherited from a parent.[3]

However, with improved recognition, more familial cases are being identified.[3]

## What are the signs and symptoms?

Individuals may experience progressive motor and cognitive dysfunction, a loss of independence and the inability to control muscles for swallowing, airway protection and purposeful movements.[9]

Symptoms are **highly variable**, although some are more common depending on the age of onset.[8]

### Common symptoms in earlier age of onset (<4 years old) individuals:[8,9]

- Delayed intellectual development or intellectual disabilities
- Delayed physical development (delayed motor skills or loss of acquired motor skills)
- Gastrointestinal issues including recurrent vomiting
- Seizures
- Enlarged head size (macrocephaly)
- Difficulty gaining weight

### Common symptoms in later age of onset (>4 years old) individuals:[9,10]

- Speech problems
- Difficulty swallowing
- Poor coordination, gait issues and loss of mobility
- Scoliosis
- Autonomic dysfunction including bladder abnormalities

## How is AxD diagnosed?

Doctors look for signs of AxD through a **combination of clinical presentation and brain magnetic resonance imaging (MRI) findings.**[2]

**A genetic test for pathogenic variants in the *GFAP* gene is usually needed to make the diagnosis.**[2]

Clinical diagnosis is challenging because **symptoms and MRI findings can vary** and mimic other more common neurological conditions (like multiple sclerosis), which can lead to **delayed diagnosis or misdiagnosis**.[3]

**Brain MRIs typically show:**

Frontal white matter abnormalities in individuals with earlier age of onset.[7,11,12]

Lesions or shrinkage of the brainstem, cerebellum and/or cervical spinal cord in individuals with later age of onset.[7,11,12]

Given the **disease's progressive nature, prompt diagnosis is critical** to allow for earlier interventions that **may improve quality of life** through reduced symptom severity.[2]

## What is the current standard of care for AxD?

While there are no standard validated assessments specific to AxD, the below measures can be useful for monitoring motor function at various disease stages:[10]

- **Vineland Adaptive Behavior Scales (VABS)** a caregiver-reported questionnaire that measures an individual's everyday adaptive skills.[13]
- **10-Meter Walk Test (10-MWT)** a clinician-administered test where walking speed is measured over 10 meters.[14]
- **Gross Motor Function Measure-88 (GMFM-88)** a clinician-scored assessment of gross motor abilities based on observed performance of standardized tasks.[15]

**There is currently no disease modifying therapy available to treat the underlying cause of AxD.[3]**

Instead, current treatment approaches are focused on symptom management and do not impact the course of disease.[2,10] This includes engaging a multidisciplinary care team to mitigate the physical (e.g., seizures, dysphagia, mobility), psychiatric and cognitive difficulties.[2,10]

Learn more about AxD at **EndAxD.org** or **ULF.org**

### References


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