



### What is Alexander disease?

**Alexander disease is a type of leukodystrophy.**

Leukodystrophies are a group of genetic conditions that mainly affect the white matter of the brain and spinal cord. The white matter is the wiring network of the brain that connects different brain regions and links the brain to the spinal cord and rest of the body.

Alexander disease affects the fatty material (myelin) that forms an insulating wrapping (sheath) around certain nerve fibers (axons). All individuals diagnosed with Alexander disease have abnormal protein aggregates only seen under the microscope known as “Rosenthal fibers” throughout certain regions of the brain and spinal cord.

### What are the symptoms seen in Alexander disease?

**Symptoms vary between types, depending upon age of onset. The symptoms are also seen as a continuum with no rigid classification between the groups.**

#### 1) Type I form (neonatal and infantile onset):

- A failure to grow and gain weight at the expected rate.
- Delays in the development of certain physical, mental, and behavioral.
- Sudden episodes of uncontrolled seizures.
- Additional features typically include rapid growth of the head, increased muscle stiffness (spasticity), lack of coordination and vomiting and difficulty swallowing, coughing, breathing, or talking.
- No single symptom or combination of symptoms is always present.

#### 2) Type II forms (juvenile and adult onset):

- Most individuals have an uneventful childhood with no symptoms or neurological signs.
- ~50% develop signs such as swallowing or speech difficulty, vomiting, muscle stiffness and restrictive movement.
- Mental function often slowly declines, although in some cases the intellectual skills remain intact.
- There is involvement of the brainstem, and the percentage of white matter loss is lesser compared to other types, but the deposition of Rosenthal fibers is largely increased.

### What causes Alexander disease?

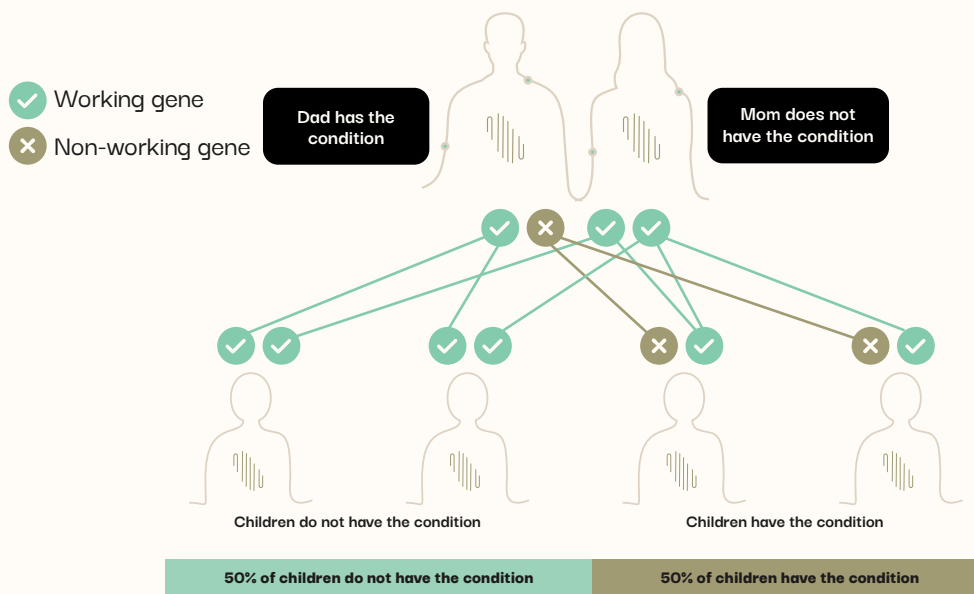
Changes in the *GFAP* gene cause Alexander disease. The *GFAP* gene provides instructions for making a protein called glial fibrillary acidic protein. Changes in the *GFAP* gene result in an accumulation of the GFAP protein and forming of Rosenthal fibers, which affects the formation and maintenance of the myelin sheath.

## How is Alexander disease diagnosed?

- MRI brain shows a number of characteristic abnormalities, predominantly in the white matter.
- Genetic testing to pick up any disease-causing changes in the *GFAP* gene.

## How is Alexander disease inherited?

- Alexander disease follows autosomal dominant inheritance, however most cases are not inherited and arise in the affected person due to random chance (de novo).
- In saying so, the risk of having an adult-onset variant or a milder form of the disease in either parent cannot be excluded.
- This disease might cause an array of symptoms and the disease progression is not the same for every person with the condition.
- For an individual who has a mutation in *GFAP* gene, the chance of developing some form of disease over their lifetime is almost 100%.



## Support and resources:

- **Elise's Corner** [elisescorner.com](http://elisescorner.com)
  - **End AxD** [endaxd.org](http://endaxd.org)
  - **Grayson's Ladder** [graysonsladder.org](http://graysonsladder.org)
  - **United Leukodystrophy Foundation Alexander Disease Video** [youtube.com/watch?v=hV92rYGd67s](https://youtube.com/watch?v=hV92rYGd67s)
  - **Leukodystrophy Australia** [leuko.org.au/](http://leuko.org.au/)
  - **Mission Massimo Foundation** [missionmassimo.com/](http://missionmassimo.com/)
  - **Hunter's Hope** [huntershope.org/familycare/leukodystrophies/](http://huntershope.org/familycare/leukodystrophies/)
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## Research:

- **Australian Leukodystrophy Clinical and Research Program** [leukonet.org.au](http://leukonet.org.au)
- **Clinical trials**  
[clinicaltrials.gov/ct2/results?cond=alexander+disease&term=&cntry=&state=&city=&dist=](https://clinicaltrials.gov/ct2/results?cond=alexander+disease&term=&cntry=&state=&city=&dist=)
- **Global Leukodystrophy Initiative** [theglia.org](http://theglia.org)

## References:

- [huntershope.org/family-care/leukodystrophies/alexander-disease](http://huntershope.org/family-care/leukodystrophies/alexander-disease)
- [rarediseases.org/rare-diseases/alexander-disease](http://rarediseases.org/rare-diseases/alexander-disease)
- [chop.edu/conditions-diseases/alexander-disease](http://chop.edu/conditions-diseases/alexander-disease)
- [ulf.org/leukodystrophies/alexander-disease](http://ulf.org/leukodystrophies/alexander-disease)