ALD - Adrenoleukodystrophy

What is Adrenoleukodystrophy?
Adrenoluekodystrophy (ALD) is also known as X-linked adrenoleukodystrophy (XALD). It is a condition which mainly affects the nervous system and the adrenal glands. The myelin that covers or insulates the nerves in the brain and the spinal cord, is susceptible to deterioration. This is called demyelination, and reduces the nerves ability to relay information to the brain. Individuals who are affected by ALD also experience damage to the outer layer of the adrenal glands (the adrenal cortex). This consequently causes a shortage of particular hormones, which is referred to as adrenocortical insufficiency.

There are three different types of ALD; Childhood Cerebral Demyelinating form, an adrenomyeloneuropathy (AMN), and a form called Addison disease only.

Due to the way that ALD is inherited, it mostly affects males.

What is the ABCD1 gene?
The ABCD1 gene provides instructions for the production of the adrenoleukodystrophy protein (ALDP). Mutations or changes in the ABCD1 gene result in a deficiency of ALDP. ALDP is located in the membranes of cell structures called peroxisomes. ALDP brings a group of fats called very long-chain fatty acids (VLCFAs) into peroxisomes, where they are broken down. Therefore, where there is a deficiency of ALDP, VLCFAs are not broken down and begin to accumulate in the body. This build up of fats may be toxic to the adrenal glands, and to the myelin that surrounds many nerves.

What are the symptoms of ALD?

Childhood Cerebral Demyelinating form		Adrenomyeloneuropathy (AMN)		Addison disease only
Symptoms first appear between the ages of 4 and 10 Symptoms Symptoms begin with learning and behavioural problems. As the condition progresses, symptoms can include difficulties with reading and writing, and understanding speech. Other symptoms can include problems with sight, poor coordination, swallowing difficulties and also impaired adrenal gland functioning.		Symptoms typically first appear in early adulthood to middle age Symptoms Individuals who are affected by AMN develop stiffness and weakness in their legs, and can often experience issues with their urinary and genital tracts. Similar to the childhood cerebral demyelinating form, people with AMN can also experience changes in their cognition and behaviours.		Onset can occur any time between childhood and adulthood. Symptoms Adrenocorticol insufficiency, which includes symptoms such as loss of appetite, weight loss, nausea and vomiting, low blood pressure, dehydration, fatigue and low blood sugar levels.

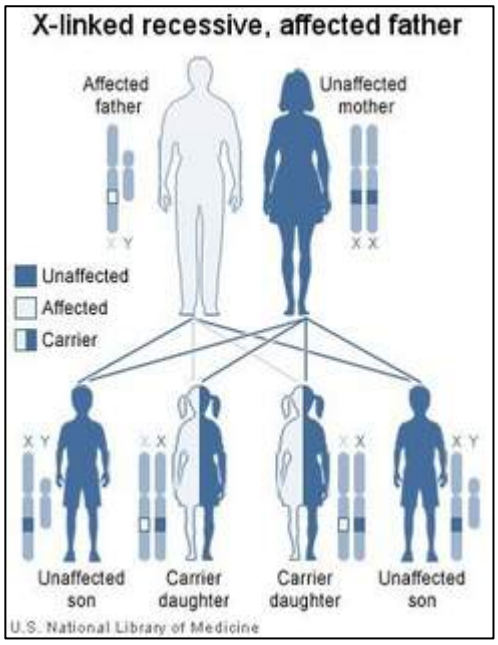
How is ALD diagnosed?

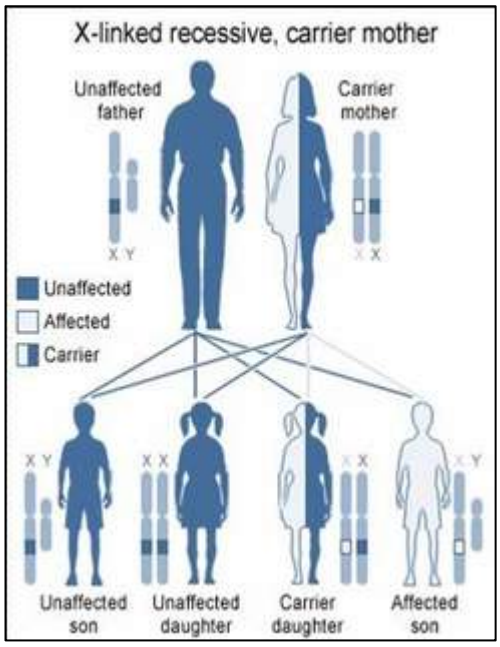
ALD is diagnosed when there is a combination of symptoms in an individual, and further investigations such as a brain MRI show typical characteristics of ALD. Genetic testing for ALD will look for changes (or mutations) in the ABDC1 gene on the X chromosome.

Are family members at risk of ALD?
ALD is an X-linked condition, meaning the affected ABCD1 gene is located on the X chromosome. As males have one X chromosome, and one Y chromosome, one copy of the affected ABCD1 gene on their only X chromosome is sufficient to cause ALD. Having two copies of X chromosomes, women who have one affected ABCD1 gene usually do not have any features of ALD, and are considered carriers. However, it has been known for women with one copy of the affected ABCD1 gene to show some signs of ALD.

Males affected with the ABCD1 gene change will always pass on the affected X chromosome to his daughters, but never to his sons, as sons will always inherit their father's Y chromosome.

Females with an X chromosome affected by a change in the ABCD1 gene have a 50/50 chance of passing the affected X chromosome to both their sons or daughters, each pregnancy.





Can ALD be treated?
While there is no cure for ALD, there are a number of treatment options.
People who have ALD and have developed adrenal insufficiency, need to have regular monitoring. Adrenal insufficiency can be effectively treated with steroids.
A stem cell transplant may be an option for some individuals. This is done by taking stem cells from bone marrow, through a bone marrow transplant. Such treatment may slow the progression of the condition, however it is not considered a cure.
Other treatments include individualised therapies for management of specific symptoms, such as medications and physical therapies to relieve muscle stiffness.

Other names for ALD

XALD

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Supports available

- Australian Addisons Disease Association:
  Website: addisons.org.au

References

Genetics Home reference
Genereviews
Australian Addisons Disease Association
United Leukodystrophy Foundation