Adrenoleukodystrophy (ALD)

A rare, inherited disease affecting the nervous system and adrenal glands.

WHAT IS ALD?

Adrenoleukodystrophy (ALD) is a rare, genetic disorder caused by pathogenic variants in the *ABCD1* gene. The body cannot properly break down very long-chain fatty acids (VLCFAs), which accumulate in the brain, spinal cord, adrenal glands, and other tissues. People with ALD are healthy at birth, but the disease course is highly variable and cannot be predicted. ALD affects approximately 1 in 15,000 people and occurs in individuals of all racial and ethnic backgrounds.

HOW IT'S INHERITED

ALD is an X-linked genetic disorder that runs in families. Because the *ABCD1* gene is located on the X chromosome, males are typically more severely affected than females and are at risk for additional disease manifestations that do not typically affect females. Regardless, females with ALD are rarely asymptomatic, with up to 90% developing symptoms in their lifetime. Fathers with ALD pass the *ABCD1* variant to all of their daughters and none of their sons. Mothers with an *ABCD1* variant have a 50% chance of passing the variant to each child, regardless of sex. When someone is diagnosed with ALD, at-risk family members should be offered genetic counseling and genetic testing, as family testing often identifies others who may benefit from early diagnosis and ongoing monitoring.

IF ALD RUNS IN YOUR FAMILY

Because ALD is an inherited disorder, a diagnosis may have implications for the entire family. Parents, siblings, children, and other at-risk relatives should be offered genetic counseling and testing. Identifying ALD early allows relatives to receive appropriate monitoring, timely treatment, and informed reproductive counseling. Some families with ALD consider reproductive options including in vitro fertilization with preimplantation genetic testing (IVF with PGT) to prevent transmission of the *ABCD1* variant.

KEY TERMS

ABCD1
The gene associated with ALD.

VLCFAS (VERY LONG-CHAIN FATTY ACIDS)
Fats that accumulate in ALD because the body cannot break them down properly.

MYELIN (WHITE MATTER)
The protective covering around nerve fibers that is damaged in cerebral ALD.

AMN (ADRENOMYELONEUROPATHY)
The most common adult form of ALD, affecting the spinal cord and peripheral nerves.

NBS (NEWBORN SCREENING)
A routine blood test performed shortly after birth that identifies babies at risk for ALD before symptoms develop.

LOES SCORE
A standardized MRI scoring system used to measure the extent and severity of cerebral ALD.

NFS (NEUROLOGIC FUNCTION SCORE)
A standardized clinical scale used to measure neurological function and disability in people with cerebral ALD.

HCT (HEMATOPOIETIC CELL TRANSPLANTATION)
Transplantation of blood-forming stem cells to treat early cerebral ALD. HCT may use stem cells from a donor (allogeneic transplant) or the patient's own genetically modified stem cells (gene therapy).

General educational information, not medical advice — always consult a qualified ALD specialist.

The Forms of ALD

ALD can present in several ways, and there's no reliable way to predict the course. A person may move between these over a lifetime.

ASYMPTOMATIC (NEWBORN SCREENING)

NO SYMPTOMS YET · MONITORED

Many children with ALD are identified through newborn screening before symptoms develop. They appear healthy at birth and show no signs of disease, but regular monitoring is essential because early detection of disease progression makes lifesaving treatment possible.

CEREBRAL ALD

BRAIN · MOST OFTEN IN BOYS AGE 3–12

An inflammatory form of ALD that destroys myelin, the protective covering of nerve fibers in the brain, and can progress rapidly. Although it most commonly occurs in childhood, it can also develop in adolescents and adults. Early signs may include changes in behavior, learning, vision, hearing, or coordination. When detected early through routine MRI surveillance, cerebral ALD can often be stabilized with a hematopoietic cell transplant (HCT) or gene therapy.

SYMPTOMATIC WOMEN

ADULTS · OFTEN IN 30S–40S

Up to 90% of women with an *ABCD1* variant will develop symptoms, usually starting in their 30s or 40s. The most common presentation is a slowly progressive myelopathy similar to adrenomyeloneuropathy (AMN), causing leg stiffness or weakness, numbness or pain, balance problems, and bladder dysfunction. Cerebral ALD and adrenal insufficiency are rare in women.

PRIMARY ADRENAL INSUFFICIENCY

ADDISON'S DISEASE · ADRENAL GLANDS

Adrenal insufficiency (Addison's disease): This is often the first sign of ALD in males. The adrenal glands do not produce enough essential hormones and can cause fatigue, weight loss, darkening of the skin, salt craving, low blood pressure, and vomiting. If left untreated, adrenal insufficiency can become life-threatening, but it can be effectively managed with daily hormone replacement therapy. AI is rare in females but has been reported, and adrenal labs should be checked in females if symptomatic.

ADRENOMYELONEUROPATHY (AMN)

SPINAL CORD · ADULTHOOD

The most common adult form of ALD, characterized by slowly progressive disease affecting the spinal cord and peripheral nerves. Symptoms often begin in a man's 20s to 40s and include leg stiffness and weakness, difficulty walking and maintaining balance, and bladder, bowel, or sexual dysfunction. Men with AMN remain at risk for cerebral ALD and adrenal insufficiency, so yearly monitoring should continue. Treatment for AMN is supportive, but clinical trials may be available.

WHY EARLY DETECTION MATTERS

Adrenal insufficiency can be life-threatening if it goes unrecognized, and cerebral ALD can only be treated successfully in its earliest stages. Newborn screening, prompt diagnosis, and regular monitoring make it possible to detect these complications early, when treatment is most effective and can preserve function and save lives.

QUESTIONS OR COMMENTS?
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