Newborn Screening for
X-linked Adrenoleukodystrophy:
Information for Parents

Baby boy
with elevated VLCFA
and no gene mutation

NEW YORK STATE | Department of Health | Wadsworth Center

What is adrenoleukodystrophy (ALD)?

ALD is one of over 40 disorders included in newborn screening in New York State. It is a rare genetic disorder. People with ALD are unable to breakdown a component of food called very long chain fatty acids (VLCFA). If VLCFA are not broken down, they build up in the body and cause symptoms.

How does New York State screen for ALD?

NYS screens for ALD by measuring the amount of a specific VLFCA (C26:0) in a sample of the baby's blood. If VLCFA are elevated on the newborn screen, then genetic testing is done to look for a mutation in the *ABCD1* gene. A mutation in the *ABCD1* gene causes ALD.

My baby boy had a positive newborn screen for ALD. Does he have ALD?

Because a gene mutation was not found, your baby boy probably does not have ALD. A gene mutation is identified in 99% of boys with ALD.

What is newborn screening?

Newborn screening involves laboratory testing on a small sample of blood collected from newborns' heels. Every state has a newborn screening program to identify infants with rare disorders, which would not usually be detected at birth. Early diagnosis and treatment of these disorders often prevents serious complications.

What else could cause a positive screen besides ALD?

The VLCFA are broken down in a part of the cell called the peroxisome. Increased VLCFA in the blood can be caused by peroxisomal disorders other than ALD. It is also possible for a baby to have a positive newborn screen for ALD, have normal repeat VLCFA and be healthy.

How do I find out if my baby boy has ALD or another peroxisomal disorder?

Your doctor will ask you to take your baby to see a special doctor, called a biochemical geneticist because they are experts at diagnosing peroxisomal disorders. Additional blood tests will be ordered by the specialist to find out if your baby has a peroxisomal disorder. **The additional tests are very important.**

What are the symptoms of ALD?

There are usually no clues at birth that a baby has ALD. X-linked ALD occurs in males. The symptoms of ALD can be different from one boy to the next. The disorder is called adrenoleukodystrophy because symptoms may involve the adrenal glands and a brain abnormality called leukodystrophy. The adrenal glands are responsible for producing the hormones that respond to stress. A low level of these hormones can happen in boys with ALD and is also known as Addison disease. Without treatment, symptoms of Addison's disease include vomiting, fatigue, low blood pressure, weakness, increased skin pigmentation and coma. Leukodystrophy is a loss of the protective coating ("white matter") around the nerves that make up the brain. Boys with X-linked ALD may develop leukodystrophy during childhood that causes increasing loss of developmental skills, seizures and eventually death. About 1/3 (30%) to ½ (50%) of boys with ALD develop leukodystrophy anytime from 3 to 21 years of age.

What is the treatment for ALD?

Boys with ALD should regularly see doctors specializing in Neurology and Endocrinology. They will need to have a brain study called an MRI every year and blood tests to check their adrenal hormones every six months. Boys with adrenal symptoms are treated with steroid hormone replacement therapy as soon as the hormone blood tests are abnormal. As soon as leukodystrophy can be seen on a brain study (MRI), boys are treated with a hematopoietic stem cell transplant (HSCT). Because HSCT is a very serious medical procedure, it is not done unless there are signs of leukodystrophy. A dietary supplement, Lorenzo's oil, in conjunction with a special diet lowers very long chain fatty acids and its role as a preventative treatment is under investigation.

No one else in my family has ALD. Is it still possible for my baby to have the condition?

Even if no one in your family has ALD, it is possible for your baby to have the condition. If your baby is diagnosed with ALD, your doctor will suggest genetic counseling to discuss the chance for your other family members to have ALD.

What are peroxisomal disorders?

Peroxisomal disorders are rare genetic conditions. People with peroxisomal disorders are unable to breakdown a component of food called very long chain fatty acids (VLCFA). The VLCFA are broken down in a part of the cell called the peroxisome. The peroxisome's job in the cell is to breakdown some components of food so the body can use it for energy and to make other substances needed by the body.

In Zellweger spectrum disorders (ZSD), the peroxisomes are either missing from the cell or there are too few of them. In other peroxisomal disorders, an enzyme in the peroxisome is not functioning (acyl-CoA oxidase deficiency and D-bifunctional protein deficiency).

How do I find out if my daughter has a peroxisomal disorder?

Your doctor will ask you to take your baby to see a special doctor, called a biochemical geneticist because they are experts at diagnosing peroxisomal disorders. Additional blood tests will be ordered by the specialist to find out if your baby has a peroxisomal disorder. **The additional tests are very important.**

What are the types of peroxisomal disorders?

There are different types of peroxisomal disorders. Zellweger spectrum disorder is used to describe a group of three conditions including Zellweger syndrome (ZS), neonatal adrenoleukodystrophy (NALD) and infantile refsum disease (IRD). Peroxisomal disorders also include acyl-CoA oxidase deficiency and D-bifunctional protein deficiency. Even though these disorders have different names, the symptoms are similar.

What are the symptoms of peroxisomal disorders?

Zellweger syndrome is the most severe ZSD. Children with ZS usually haves symptoms at birth. Their symptoms include very low muscle tone, poor feeding, seizures, hearing loss, vision loss and liver cysts. Newborns with ZS may also have a bone abnormality in their knees and legs called chondrodysplasia punctata. Newborns with ZSD usually have a flattened appearance to their face with a broad nose. Most babies with ZS die in the first year of life.

The symptoms of NALD and IRD are similar to ZS, but less severe. Symptoms usually begin after the newborn period. The age symptoms are first noticed and the severity of symptoms is variable. Children with NALD and IRD may have a severe disorder including low muscle tone, seizures, hearing loss, vision loss and liver cysts. They may also have episodes of bleeding (hemorrhage), which can happen in the brain. Children with NALD and IRD usually have developmental delay and some will never learn to walk and talk. Some children with NALD and IRD develop a condition in their brain called leukodystrophy. In leukodystrophy, the protective coating around the nerves in the brain (myelin) is slowly lost. Children with leukodystrophy lose developmental skills and eventually it causes their death.

Rarely, some children with NALD and IRD may have milder symptoms. They learn to walk and talk later than other children (developmental delay) and may have hearing/vision problems, but otherwise are healthy.

D-bifunctional protein deficiency and acyl-CoA oxidase deficiency are both very rare disorders. The symptoms are similar to ZSDs. Most children with these disorders die in early childhood.

What is the treatment for peroxisomal disorders?

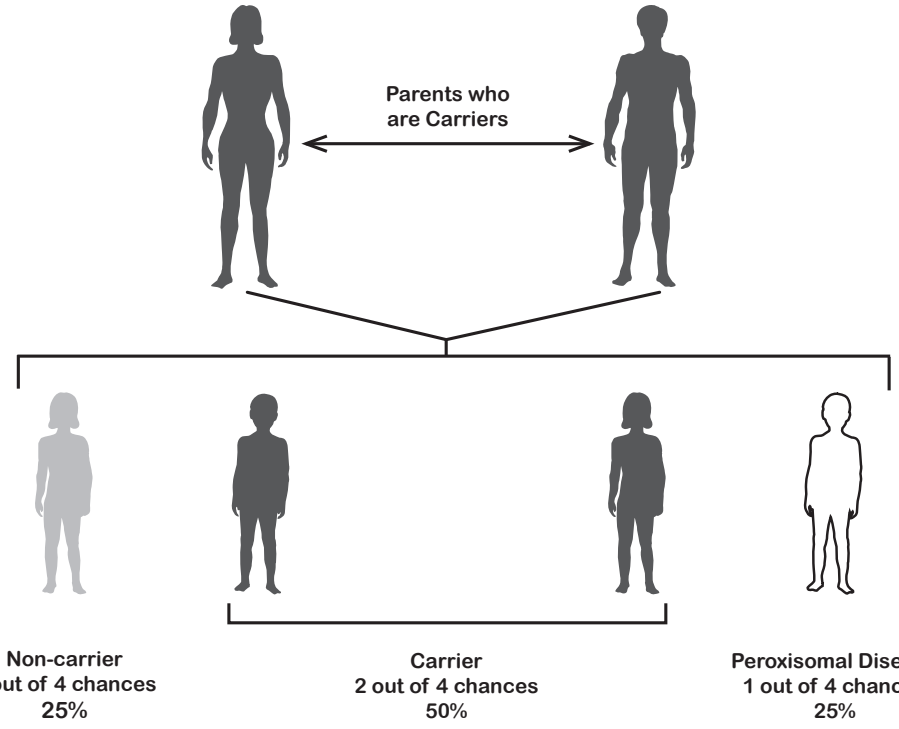
Unfortunately, there is not a treatment for peroxisomal disorders. If a peroxisomal disorder is identified early, doctors can watch for the possible symptoms and monitor nutrition, bones, liver, hearing, vision and development. Depending on symptoms, interventions may include high calorie formula, glasses, hearing aides, seizure medication, developmental therapies and vitamin K for liver disease.

What is the chance for other family members to inherit a peroxisomal disorder?

Mutations in one of several genes cause peroxisomal disorders. Each parent of a newborn with a peroxisomal disorder typically has one functional and one mutated gene and is considered a carrier. When both parents are carriers, the chance of a newborn inheriting two mutated genes is 25%.

Who can I call if I have additional questions about newborn screening for ALD?

Your baby's doctor and the NYS Newborn Screening Program are resources for additional questions about newborn screening for ALD.



Wadsworth Center's
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