



## Newborn Screening FACT Sheet

# X-linked Adrenoleukodystrophy (X-ALD)

### What is Adrenoleukodystrophy (X-ALD)?

Adrenoleukodystrophy occurs when the body's cells cannot break down very long-chain fatty acids (VLCFAs). These build up and cause problems in the brain, spinal cord and adrenal glands.

If a baby's screening result for ALD is out of the normal range, the baby's doctor will recommend additional testing. **It is important to remember that an out-of-range screening result does not necessarily mean that a baby has the condition.** But follow-up with a medical specialist is very important.

### What Causes X-ALD?

X-ALD is caused by changes (usually referred to as variants) in the ABCD1 gene. This gene provides instructions for making the adrenoleukodystrophy protein (ALDP). The ALDP binds to VLCFAs and carries them to the area of the cell where they get broken down.

When the ABCD1 gene has a pathogenic variant, the ALDP is either abnormal or missing. The VLCFAs build up in the cell, causing damage to the brain, spine and adrenal glands.

The ABCD1 gene is located on the X chromosome. Females have two X chromosomes in each cell. Males have one X chromosome and one Y chromosome. One variant copy of the ABCD1 gene is enough to cause X-ALD in boys.

Females with one non-working copy of the gene and one working copy are referred to as carriers, but may also develop symptoms of X-ALD as adults.

There are three types of X-ALD: Childhood Cerebral, adrenomyeloneuropathy (AMN), and Addison's disease. Newborn screening tests are not able to identify which of the three types a baby will have.

### What Symptoms Occur with X-ALD?

There are usually no symptoms of X-ALD at birth. Symptoms of X-ALD can be different depending upon the type of X-ALD, and the age and sex of the person. Common symptoms for the different types of X-ALD include:

#### Childhood Cerebral

This most severe type of X-ALD occurs in male patients, starting with mild symptoms that may look like Attention Deficit Hyperactivity Disorder (ADHD). Over weeks or months, symptoms become more severe and may include behavior and learning disabilities, seizures, weakness, vision loss, and hearing loss. If untreated, this form is fatal.

#### Adrenomyeloneuropathy (AMN)

Symptoms of AMN will not usually begin until adulthood. Patients develop leg weakness that may worsen with time, and may experience problems with the bladder and/or the genital tract. About 20 percent of individuals with AMN will develop cerebral symptoms.

#### Addison's disease (Adrenal Insufficiency)

If untreated, males with Addison's disease will develop adrenal symptoms including vomiting, fatigue, low blood pressure, weakness, skin darkening, and coma. These symptoms can develop as early as the first year of life and must be treated immediately.

#### Asymptomatic X-ALD

For some boys, it may take many years for symptoms to appear. Even if a baby/child does not have symptoms of ALD, it is important for him to be regularly checked by a neurologist and an endocrinologist.

#### Female Carriers

More than 50 percent of women who are carriers show some symptoms of X-ALD. These often appear later in life than in men and are usually milder, but may be severe. Some women may never show any symptoms. Adrenal insufficiency is not typically seen in women. Not all female carriers have abnormal levels of VLCFA's.

### What is the Treatment for X-ALD?

X-ALD can be treated. Possible treatments include:

#### Stem cell transplant

This treatment may halt the progression of Childhood Cerebral X-ALD if diagnosed and treated early.

#### Steroids

Individuals who have adrenal insufficiency can be treated effectively with replacement corticosteroids.

#### Other treatments

Other treatments may include medication to relieve symptoms like stiffness and seizures; physical therapy, which can help relieve muscle spasms and reduce muscle rigidity, and experimental dietary therapies.

#### Gene therapy

Clinical trials using gene therapy on boys with Childhood Cerebral X-ALD are promising and may be another method to stop disease progression.