

# LYSOSOMAL ACID LIPASE DEFICIENCY TESTING



## What is lysosomal acid lipase deficiency?

Lysosomal acid lipase (LAL) deficiency is a rare, inherited condition that affects the body's ability to break down fats and cholesterol (lipids). It results in the buildup of very large amounts of lipids inside organs and tissues throughout the body.

LAL deficiency can occur in infants, children, adolescents, and adults. The type that occurs during infancy is called Wolman disease. Shortly after birth, infants with Wolman disease may develop some of the following signs and symptoms<sup>1-3</sup>:

- Swelling or bloating of the abdomen (abdominal distention)
- Liver and spleen enlargement
- Yellowing of the skin and eyes (jaundice)
- Calcium deposits on the adrenal glands
- Forceful vomiting, frequent diarrhea, and foul smelling, fatty stools
- Failure to gain weight and grow
- Inability to absorb nutrients from food (malnutrition)

Without treatment, infants with Wolman disease often die within the first year of life.<sup>1-3</sup>

The type of LAL deficiency that occurs in children, adolescents, and adults is called cholesteryl ester storage disease (CESD).

- CESD progresses more slowly than Wolman disease, may cause mild symptoms or no symptoms at all, and may go undiagnosed until later in life.<sup>1,4</sup>
- It can lead to liver inflammation and damage (cirrhosis), liver failure, and early death.<sup>1,4,5</sup> It may also cause an increased risk for early-onset heart disease due to the buildup of lipids inside the walls of blood vessels.<sup>1,6</sup>

- It may be managed with a low-fat (cholesterol and triglycerides) diet and cholesterol-lowering medications, but the disorder can not be cured. If liver failure occurs, liver transplantation may be an option.<sup>1,4</sup>

### Is there a treatment for LAL deficiency?

Enzyme replacement therapy (ERT) with sebelipase alpha became available in 2015 for the treatment of patients of all ages.

### What causes LAL deficiency?

LAL deficiency is caused by abnormal changes in a gene. Genes are found in every cell in your body. They carry the instructions for making proteins that control how each of your cells work. Genes can undergo abnormal changes (called mutations) that may cause cells to stop working the way they should. Gene mutations may result in health problems, and they may be passed from parent to child (inherited).

The *LIPA* gene contains instructions for making lysosomal acid lipase, a protein that helps cells break down lipids so they can be used by the body and carried to the liver for removal. When the *LIPA* gene is altered, cells may make little or no LAL, or the LAL that is made will not work properly. This keeps the body from using lipids properly and causes very large amounts of lipids to build up inside organs and tissues.

### How is LAL deficiency inherited?

Normally, each of your cells carries 2 copies of all your genes. You inherit 1 copy of a gene from each of your parents. LAL deficiency disorder is inherited in an autosomal recessive manner.<sup>1,3,4</sup> This means a child must inherit 2 copies of a *LIPA* mutation (1 copy from each parent) in order to be affected with LAL deficiency.

People who carry 1 *LIPA* mutation are not affected with LAL deficiency. However, when 2 people who are carriers of *LIPA* mutations have children, there is a 1 in 4 (25%) chance with each pregnancy that the child will inherit both copies of the mutation and be affected with LAL deficiency.

## How is LAL deficiency diagnosed?

Diagnosing LAL deficiency begins with a physical exam, medical history, and laboratory tests, such as cholesterol testing and liver function tests. A blood test that detects low or absent levels of the LAL enzyme may be used to confirm a diagnosis of LAL deficiency.<sup>3,4,6</sup>

*LIPA* full gene sequencing is a procedure that reads the instructions (DNA) that make up the *LIPA* gene. This is a way to identify the presence of altered *LIPA* genes in a person's cells, helping a doctor confirm the diagnosis of LAL deficiency. The test can be performed on a sample of blood or prenatal samples of amniotic fluid (the watery substance that surrounds a fetus) or the chorionic villi (a small piece of tissue taken from the placenta).<sup>3</sup>

## What possible results of enzyme testing can be reported, and what might they mean?

- **Unaffected:** The enzyme level falls within the unaffected range. This result would rule out a diagnosis of LAL deficiency.
- **Affected:** The enzyme level is absent or low enough to indicate an affected individual. This result would confirm a diagnosis of LAL deficiency.
- **Intermediate:** The enzyme level falls between the affected and unaffected ranges. The interpretation of this result may vary depending on the enzyme level and available clinical information.

Test results should be combined with clinical findings and reviewed by a health professional who specializes in medical genetics.

**Note:** This material is provided for general information purposes only. It is not intended as a substitute for medical advice and/or consultation with a physician or technical expert.

## References

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6. Hamilton, J., Jones, I., Srivastava, R. and Galloway, P. A new method for the measurement of lysosomal acid lipase in dried blood spots using the inhibitor Lalstat 2. *Clinica Chimica Acta*. 2012;413:1207-1210.

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## Where can I find more information?

If you have questions or want more information about testing for LAL deficiency, ask your doctor or genetic counselor. You may search for a genetic counselor in your area using an online address book provided by the National Society of Genetic Counselors at [www.nsgc.org](http://www.nsgc.org).

Other information resources include:

## Where can I find more information?

- Genetics Home Reference  
Home page: <http://ghr.nlm.nih.gov>