

### What is dihydrolipoamide dehydrogenase deficiency?

Dihydrolipoamide dehydrogenase deficiency is an inherited disease of variable onset and severity, characterized by recurrent episodes of vomiting, abdominal pain, and encephalopathy (general brain dysfunction).<sup>1</sup> The enzyme dihydrolipoamide dehydrogenase is responsible for the breakdown of three amino acids present in many kinds of protein-rich foods: leucine, isoleucine, and valine. Symptoms are due to the toxic accumulation of these amino acids in the brain and other organs.<sup>2</sup> Dihydrolipoamide dehydrogenase deficiency is also known as maple syrup urine disease type III, E3-deficient maple syrup urine disease, and lipoamide dehydrogenase deficiency.<sup>3</sup>

### What are the symptoms of dihydrolipoamide dehydrogenase deficiency and what treatment is available?

The symptoms and onset of dihydrolipoamide dehydrogenase deficiency vary considerably. A severe form is characterized by neonatal onset and progressive symptoms, while onset in early childhood or adulthood has been associated with normal neurological development.<sup>1,4</sup>

Dihydrolipoamide dehydrogenase deficiency is characterized by recurrent episodes that include:<sup>1,4</sup>

- Vomiting
- Abdominal pain
- Encephalopathy (brain dysfunction), sometimes triggering temporary lack of coordination, seizures, blindness, confusion, and coma
- Metabolic crisis that can be life threatening

While some patients may be asymptomatic between attacks, experiencing only fatigue with exertion, other patients may have:<sup>1,4</sup>

- Persistent lactic acidosis (toxic build-up of lactic acid in tissues), leading to organ failure
- Hepatomegaly (enlarged liver)
- Neurological impairment, presenting as developmental delay, intellectual disabilities, lack of coordination, low muscle tone, and weakness

There is no cure for dihydrolipoamide dehydrogenase deficiency. Dietary treatment involves lifelong restriction of the amino acids that cannot be broken down, starting as early as possible. Unfortunately, dietary modifications are not always effective.<sup>3</sup>

### How is dihydrolipoamide dehydrogenase deficiency inherited?

Dihydrolipoamide dehydrogenase deficiency is an autosomal recessive disease caused by mutations in the *DLD* gene.<sup>2</sup> An individual who inherits one *DLD* mutation is a carrier and is not expected to have related health problems. An individual who inherits two *DLD* mutations, one from each parent, is expected to be affected with dihydrolipoamide dehydrogenase deficiency.

If both members of a couple are carriers, the risk for an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

### Who is at risk for dihydrolipoamide dehydrogenase deficiency?

DLD is a rare disorder most frequently reported in individuals of Ashkenazi (Eastern European) Jewish ancestry but occurring in other populations as well.<sup>5</sup> The carrier frequency of dihydrolipoamide dehydrogenase deficiency in the Ashkenazi Jewish population is approximately 1 in 107.<sup>6</sup>

Having a relative who is a carrier or is affected can increase an individual's risk to be a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

### What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

### What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

### Where can I get more information?

Jewish genetic diseases: <http://www.mazornet.com/genetics/dld.htm>

Genetics Home Reference: <http://ghr.nlm.nih.gov/condition/dihydrolipoamide-dehydrogenase-deficiency>

### References

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