

---

# $\beta$ -Ketothiolase (BKT) Deficiency – Organic Acid Disorders

---

## What are organic acid disorders?

Organic acid disorders (also sometimes called organic acidemias) are a class of inherited metabolic disorders that occur when the body cannot break certain components of proteins (for example, branched-chain amino acids) and other substances. This leads to an accumulation of harmful substances in the blood and urine, which can cause serious health problems.

## What is $\beta$ -Ketothiolase Deficiency?

In the body, the breakdown of protein produces isoleucine and other amino acids. Isoleucine is further processed by an enzyme called  $\beta$ -Ketothiolase (also called 'mitochondrial acetoacetyl-CoA thiolase'). BKT deficiency occurs when this enzyme is not working well or is missing. This leads to the accumulation of harmful substances in the blood.

## What is its incidence?

BKT deficiency is a rare disease. The incidence is unknown.

## What causes the disease?

Mutations in the gene for  $\beta$ -Ketothiolase, called ACAT1, results in enzyme that is not working well or is deficient.

## What are the clinical features of the disease?

Although babies with BKT deficiency are usually normal at birth, an episode of metabolic crisis leading to coma and death can be triggered by an illness or going without food for too long. The first episode usually occurs during the first two years of life.

Increased amounts of acidic substances are generally found in the blood (acidemia) during a crisis. Other symptoms include lethargy, failure to thrive, vomiting, abnormally high or low muscle tone. In the long term, repeated episodes may cause brain damage and learning problems or mental retardation.

The presentation of BKT deficiency is variable and there may be individuals with the disorder who are asymptomatic or do not develop symptoms until later in life.

## How is the diagnosis confirmed?

The diagnosis of BKT deficiency is confirmed by looking for specific substances in the blood and urine. A specific urine organic acid profile, a specific acylcarnitine profile, the finding elevated levels of ketones in the blood and urine, and the finding of increased amounts of ammonia and glucose are all helpful in confirming the diagnosis. Enzyme studies and mutation analysis of the ACAT1 gene may also assist in confirming the diagnosis. Diagnostic testing is arranged by specialists at your regional treatment centre.

## What is the treatment of the disease?

Patients with BKT deficiency should avoid going long periods without food. Supplementation with carnitine may also be considered. A low protein and/or low fat diet is often recommended in children with BKT deficiency. In an acute symptomatic episode, IV glucose and fluids are given. Treatment is coordinated by specialists at your regional treatment centre.

## What is the outcome of treatment?

If treatment is able to prevent episodes of metabolic crisis, children with BKT deficiency have a good prognosis. However, response to treatment and therefore the outcome is variable.

## Can a family have more than one child with BKT Deficiency?

BKT deficiency is inherited as an autosomal recessive disorder. The parents of a child who has BKT deficiency are assumed to be carriers for the disorder and have a 1 in 4 (25%) chance, in each pregnancy, of having another child with the disorder. Prenatal testing for BKT deficiency can be done as early as 10-12 weeks of pregnancy. Genetic counselling to discuss the benefits of prenatal testing options in more detail is recommended.

Unaffected siblings of a child with BKT deficiency have a 2/3 chance of being carriers. Carriers are healthy and do not have symptoms of BKT deficiency.

### Resources

<http://www.newbornscreening.info/Parents/organicaciddisorders/BKD.html>

<http://www.oaanews.org/>

<http://www.geneclinics.org/>