



3MCC Deficiency Information for Health Professionals

3-Methylcrotonyl-CoA Carboxylase deficiency (3MCC deficiency) is an organic acid disorder in which individuals are unable to process leucine.

✓ Clinical Symptoms

Symptoms start after 3 months of age in some individuals; others will never have symptoms. 3MCC deficiency can cause metabolic crises, particularly after fasting, illness/infection, or high protein intake. Symptoms of a metabolic crisis include feeding difficulties, vomiting, behavioral changes, hypotonia, lethargy, hypoglycemia, metabolic acidosis, increased ketones in urine, and high levels of ammonia in the blood. If untreated, the crisis can lead to breathing problems, liver failure, seizures, coma, and death. Repeat crises can cause brain damage.

Even without a metabolic crisis, symptoms may include poor growth and development, and hypotonia or spasticity. Adulthood symptoms include weakness and lethargy.

✓ Incidence

3MCC deficiency occurs in greater than 1 in 75,000 births.

✓ Genetics of 3MCC deficiency

Mutations in the MCCC1 and MCCC2 genes cause 3MCC deficiency. Mutations in these genes prevent or reduce the production of the enzyme 3-methylcrotonyl-CoA carboxylase, which is necessary for the processing of leucine. Mutations, therefore, cause a buildup of the byproducts of leucine processing in the body.

✓ How do people inherit 3MCC deficiency?

3MCC deficiency is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with 3MCC deficiency, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Many children identified through newborn screening will not require treatment. If individuals show symptoms of 3MCC deficiency, treatment is necessary for normal growth and development. Individuals may need a diet low in leucine and protein. L-carnitine supplementation may be beneficial and individuals should avoid fasting.

✓ **Screening Methodology**

Primary screening for 3MCC deficiency utilizes tandem mass spectrometry. Individuals who screen positive for 3MCC deficiency will have elevated levels of C5-OH (3-hydroxyisovaleryl carnitine). False positive and false negative results are possible with this screen.

✓ **What to do After Receiving Presumptive Positive 3MCC Deficiency Screening Results**

- 1) The clinician should immediately check on the clinical status of the baby.
- 2) Consultation with a metabolic specialist is essential.
- 3) Call KS Newborn Screening Program at 785-291-3363 with questions about results.
- 4) Report clinical findings to the Newborn Screening Program at 785-291-3363.
- 5) Same birth siblings (twins, triplets) of infants diagnosed with 3MCC deficiency should be re-screened; additional testing of these siblings also may be indicated.
- 6) Consider testing older siblings of affected individuals. Many individuals may have no symptoms of this condition and may be undiagnosed. Maternal 3MCC deficiency may also need to be excluded.

✓ **Confirmation of Diagnosis**

The diagnosis of 3MCC deficiency is confirmed through urine organic acid analysis and plasma acylcarnitine analysis.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive 3MCC deficiency newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with 3MCC deficiency, the following points should be conveyed to parents:

- ***If treatment is required, it is likely to be life long.***
- ***Parent should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include pediatrics, metabolic specialists, and a dietician.***
- ***Genetic services may be indicated. A list of geneticists and counselors, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

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