



Carnitine Uptake Defect Information for Health Professionals

Carnitine uptake defect is a type of fatty acid oxidation disorder in which the enzyme carnitine transporter is missing or is not functioning correctly. Carnitine cannot be transported into cells leading to difficulty utilizing fats for energy.

✓ Clinical Symptoms

There are two forms of carnitine uptake defect; one beginning in infancy and one in childhood.

Symptoms of the infancy form begin between birth and age three. Metabolic crises can occur, particularly after fasting or periods of sickness/infection. Symptoms of a metabolic crisis include lethargy, behavior changes, feeding problems, diarrhea, fever, and hypoglycemia. If untreated, metabolic crisis can lead to breathing problems, brain swelling, seizures, coma, and death. If untreated, babies can also have cardiomegaly, skeletal muscle weakness, and anemia. Brain damage can result from repeated episodes of metabolic crisis.

Symptoms of the childhood form of carnitine uptake defect usually begin between the ages of 1 and 7. These children do not have metabolic crises. Symptoms of the childhood form include cardiomegaly, muscle weakness, and possibly heart failure and death if untreated.

✓ Incidence

Carnitine uptake defect occurs in less than 1 out of every 100,000 births.

✓ Genetics of carnitine uptake defect

Mutations in the OCTN2 gene cause carnitine uptake defect. Mutations in this gene cause a defect in carnitine transport across the plasma membrane and into cells. This limits acylcarnitine formation and limits energy production by preventing transport of fatty acids into the mitochondria.

✓ How do people inherit carnitine uptake defect?

Carnitine uptake defect 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 carnitine uptake defect, 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

Immediate diagnosis and treatment of carnitine uptake defect is critical to normal development and health. Treatment is usually effective if started early and continued throughout life. Recommended treatment is L-carnitine supplementation and avoidance of fasting. This treatment can reverse cardiomegaly. Individuals may benefit from a low-fat, high-carbohydrate diet.

✓ **Screening Methodology**

Primary screening for carnitine uptake defect utilizes tandem mass spectrometry. Individuals who screen positive for carnitine uptake defect will have low levels of carnitine, and very low levels of C0 (free carnitine).

✓ **What to do After Receiving Presumptive Positive CUD Screening Results**

MEDICAL EMERGENCY: TAKE THE FOLLOWING IMMEDIATE ACTIONS

- 1) **The clinician should immediately check on the clinical status of the baby.**
- 2) **Consultation with a metabolic specialist is essential.**
- 3) **The specialist may request confirmatory lab tests on the baby.**
- 4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
- 5) **Report Clinical Findings to Newborn Screening Program at 785-291-3363.**
- 6) **Same birth siblings (twins, triplets) of infants diagnosed with CUD should be re-screened; additional testing of these siblings also may be indicated.**
- 7) **Testing should be done for mothers of newborns with CUD because there have been cases of undiagnosed maternal CUD.**

✓ **Confirmation of Diagnosis**

The diagnosis of carnitine uptake defect is confirmed through plasma and urine carnitine analysis revealing a decreased level of free and total carnitine in plasma and an excess amount of carnitine in urine. Transporter analysis and gene sequencing may also be used to confirm the diagnosis.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive carnitine uptake defect 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 CUD, the following points should be conveyed to parents:

- ***Parents should understand that treatment for carnitine uptake defect will be lifelong.***
- ***Parents should understand that treatment cannot necessarily prevent all health complications. 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 the following specialties: pediatrics and metabolic disease specialists.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, 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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