

Disease Name:

CARNITINE PALMITOYLTRANSFERASE II DEFICIENCY
(MYOPATHY WITH DEFICIENCY OF CARNITINE PALMITOYLTRANSFERASE II;
CPT II DEFICIENCY, MYOPATHIC; HYPOGLYCEMIA, HYPOKETOTIC, WITH
DEFICIENCY OF CARNITINE PALMITOYLTRANSFERASE II; CPT DEFICIENCY,
HEPATIC, TYPE II)

Classification: Fatty acid oxidations disorder

**Genetic
Information:**

Inheritance: Autosomal recessive

Population Incidence: Unknown

Ethnic Incidence: No known population at increased risk

Gene & Location: CPT2 gene- 1q32

Common Mutation: Adult onset with common mutation-S113L in 60%; other forms without common mutations

OMIM # *600650; *600649; #255110

**Disease
Information:**

Symptom Onset: In the classic form onset is usually between 15 and 30 years, but can be earlier. The other forms have neonatal to childhood onset.

Symptoms: The classic form presents with episodic muscle weakness, pain and myoglobinuria usually prompted by prolonged exercise, fasting, infection, and stress or cold exposure. Lipid storage in muscle is found in 20% of patients. Permanent muscle weakness is rare but does occur, especially in proximal muscles. Renal failure from myoglobinuria is found in 25% of patients. Death may occur from renal failure or from respiratory insufficiency if the respiratory muscle are involved in an acute attack. Between episodes CK is normal. Fasting ketogenesis is decreased in some. Carnitine levels are usually normal. Cardiac dysfunction is rare. 80% of affected patients are male. The infantile form, hepatocardiomyopathy type, is very rare, with only a few cases reported. Symptoms include fasting hypoketotic hypoglycemia, hepatomegaly, coma, seizures, cardiomegaly, dysrhythmia, skeletal muscle involvement and marked lipid accumulation in muscle. Patients may survive if recognized and treated aggressively. These infants usually have dysmorphic features including cystic renal dysplasia, cataracts and neuronal migration defects, specifically brain dysplasia and/or intracerebral calcifications. These patients usually die in the first month of life.

Physical Findings: Minor facial dysmorphisms and renal dysplasia in the neonatal form

Treatment: Avoid fasting. Intravenous fluids and glucose when ill, hypoglycemic or with myoglobinuria. High carbohydrate, low fat diet. MCT oil supplement to supply the medium chains for beta-oxidation. Carnitine supplementation is controversial, as it may increase long-chain acylcarnitines and cause arrhythmia.

Natural History without treatment: In the adult/ classic form recurrent myoglobinuria may lead to renal failure and death although most patients survive. Death or disability may occur during the infantile hypoketotic hypoglycemic episodes and death has been uniform in all neonatal presentations.

Natural History with treatment: Goal is to avoid myoglobinuria and muscle pain in the classic form. Patients with the severe neonatal form are not likely to benefit from treatment.

Metabolic Information:

Missing Enzyme & Location: CARNITINE PALMITOYLTRANSFERASE II catalyzes the last step of the carnitine-dependent entry of activated long-chain fatty acids into the mitochondria for beta-oxidation. The defect is in the conversion of the long-chain acylcarnitines to their corresponding acyl-CoA's upon transport into the mitochondria. The result is accumulation of long chain acylcarnitine in the mitochondrial matrix.

MS/MS profile: C0 (free carnitine)- low
C16 (palmitoyl carnitine)- elevated
C18:1 (linoleoyl carnitine)- elevated
C16/C2 or C18/C2- elevated

Prenatal testing: DNA and enzyme analysis are available for at risk families.

Miscellaneous Information:

May be some thermolability of the mutant enzyme in the adult form and explain the episodes triggered by acute febrile illness. Some studies have looked at protective effect of estrogen on enzyme function that may be effective in the milder forms.

Prepared for the NW Regional Newborn Screening Program by Sara Copeland MD, Judith Tuerck RN MS and Lorinda Paradise at OHSU in Portland, OR.

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