

Disease Name:

**SHORT-CHAIN ACYL-COA DEHYDROGENASE
DEFICIENCY**

(ACADS DEFICIENCY; SCADH DEFICIENCY; SCAD DEFICIENCY)

Classification: Fatty acid oxidation defect

**Genetic
Information:**

Inheritance: Autosomal Recessive

Population Incidence: 1:40,000-1:100,000

Ethnic Incidence: No known population at increased risk

Gene & Location: 12q22-qter- ACADS, SCAD gene

Common Mutation: No common disease mutations have been identified. Two common SCAD “disease susceptibility” mutations (625G>A) (511C>T) are present in 14% of the general population. 69% of persons with ethymalonic aciduria are either hetero/homozygous for these susceptibility mutations.

OMIM # *606885; #201470

**Disease
Information:**

Symptom Onset: Only 20 SCAD deficient patients have been described. The majority became symptomatic in the first week-3 months of life, 4 before 24 months and two presented as adults.

Symptoms: About 50% of patients have hypotonia and developmental delay. Variable symptoms are present in patients presenting early, including seizures, respiratory distress, acidosis, poor feeding, vomiting or failure to thrive, and one death. Only one patient had hypoglycemia. Acute symptoms in most patients did not recur. Both adults presented with proximal muscle weakness associated with periods of pain, nausea/vomiting and shortness of breath.

Physical Findings: No specific dysmorphism.

Treatment: Supportive standard treatment of symptoms. Common fatty acid oxidation therapies including low fat diet, carnitine and riboflavin supplements have not improved hypotonia or developmental delay. One patient with cyclic vomiting improved on frequent feeding.

Natural History without treatment: Highly variable, from death in the neonatal period to probable asymptomatic persons. It is reassuring that some of the early onset patients completely recovered and have had normal growth and development into adulthood. Long-term outcome beyond adolescence is unknown, specifically the development of further muscle weakness. Environmental stressors are suspected to precipitate symptoms in some cases, but they are not well understood.

Natural History with treatment: There is no proven efficacy of the usual treatments for fatty acid oxidation disorders, with the possible exception of avoiding fasting.

Metabolic Information:

Missing Enzyme & Location: Short chain acyl-CoA dehydrogenase, liver, muscle and fibroblasts. SCAD is one of three enzymes that catalyze the first step in mitochondrial beta-oxidation of fatty acids four to six carbons in length.

MS/MS profile: C4 (butyryl/ isobutyryl carnitine)- elevated

Prenatal testing: If both gene mutations are known theoretically possible.

Miscellaneous Information:

Ethylmalonic acid and methylsuccinate are elevated in the urine. Maternal pregnancy complications include HELLP or acute fatty liver of pregnancy (AFLP) with some affected SCAD fetuses.

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