



Genetic Fact Sheets for Professionals

Organic Acid Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – [http:// www.newbornscreening.info](http://www.newbornscreening.info)

Disease name	Beta-ketothiolase deficiency
Alternate name(s)	Alpha-methylacetoacetic aciduria, 2-methyl-3-hydroxybutyric academi, Mitochondrial acetoacetyl-CoA thiolase deficiency, MAT deficiency, T2 deficiency, 3-oxothiolase deficiency, 3-ketothiolase deficiency, 3-KTD deficiency
Acronym	BKD
Disease classification	Organic Acid Disorder
Variants	No, but there is considerable clinical heterogeneity
Variant name	N/A
Symptom onset	Late infancy or childhood. Mean age at presentation is 15 months (range 3 days to 48 months). There are documented cases of asymptomatic patients with enzyme deficiency. Frequency of decompensation attacks falls with age and is uncommon after the age of 10.
Symptoms	Symptoms include intermittent episodes of severe metabolic acidosis and ketosis accompanied by vomiting (often hematemeses), diarrhea and coma that may progress to death. There is great clinical heterogeneity between patients. Infancy is the period of highest risk for decompensation. Death or neurologic complications can occur. Neurologic damage includes striatal necrosis of the basal ganglia, dystonia and/or mental retardation. Other symptoms include cardiomyopathy, prolonged QT interval, neutropenia, thrombocytopenia, poor weight gain, renal failure and short stature. If neurologically intact, patients are normal between episodes.
Natural history without treatment	Clinical outcome varies widely with a few patients suffering severe psychomotor retardation or death as a result of their initial attack and others with normal development and no episodes of acidosis.
Natural history with treatment	Despite severe recurrent attacks, appropriate supportive care can result in normal development.

Treatment	Avoidance of fasting. Bicarbonate therapy and intravenous glucose in acute crises. Possible protein restriction. Consider carnitine supplementation.
Other	N/A
Physical phenotype	No dysmorphisms
Inheritance	Autosomal recessive
General population incidence	Unknown
Ethnic differences	None known
Population	N/A
Ethnic incidence	N/A
Enzyme location	Mitochondria
Enzyme function	Converts 2-methylacetoacetyl-CoA to propionyl-CoA and acetyl-CoA
Missing enzyme	Mitochondrial acetoacetyl-CoA thiolase enzyme
Metabolite changes	Increased urinary excretion of 2-methyl-3-hydroxybutyric acid, 2-methylacetoacetic acid, tiglylglycine, 2-butanone, and ketone bodies (acetoacetic acid, 3-hydroxybutyric acid).
Gene	ACAT1
Gene location	11q22.3-q23.1
DNA testing available	Not in US. Sequencing of gene on a research basis.
DNA testing detail	No common mutation known
Prenatal testing	Enzyme analysis in amniocytes or CVS tissue. If mutations have been identified, DNA testing is possible.
MS/MS profile	C5:1 tiglycarnitine – elevated
OMIM link	www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=203750
Genetests link	www.genetests.org/servlet/access?prg=j&db=genestar&site=&fcn=d&id=12600&qry=22660&res=nous&res=nointl&key=Issq6RQIfI8i5&show_flag=c

Support group

Organic Acidemia Association
www.oaanews.org

Save Babies through Screening Foundation
www.savebabies.org

Genetic Alliance
www.geneticalliance.org

Document Info

Created by

www.newbornscreening.info

Reviewed by

HI, CA, OR and WA metabolic specialists

Review date

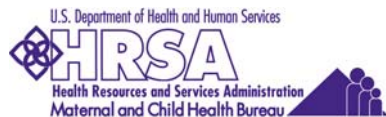
May 2, 2005

Update on

N/A

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This project is supported by a grant from the Maternal and Child Health Bureau, Health Resources and Service Administration, Genetic Services Branch, MCH Project #:1H46 MC 00189-03 <http://mchb.hrsa.gov>