

Disease Name	
BETA KETOTHIOLASE DEFICIENCY (BKT)	
<i>(ALPHA-METHYLACETOACETIC ACIDURIA; 2-METHYL-3-HYDROXYBUTYRIC ACIDEMIA; MITOCHONDRIAL ACETOACETYL-CoA THIOLASE DEFICIENCY; MAAT DEFICIENCY; T2 DEFICIENCY; 3-OXOTHIOLASE DEFICIENCY; 3-KETOTHIOLASE DEFICIENCY; 3-KTD DEFICIENCY)</i>	
Classification:	Organic aciduria and disorder of ketone body metabolism
Genetic Information	
Inheritance:	Autosomal recessive.
Population Incidence:	Unknown.
Ethnic Incidence:	No known population at increased risk.
Gene & Location:	ACAT1 gene on 11q22.3-q23.1
Common Mutation:	None, in 19 patients identified 24 mutations have been found.
OMIM #	#203750
Disease Information	
Symptom Onset:	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 hematemesis), 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.
Physical Findings:	No particular dysmorphisms.
Treatment:	Acute management of the ketoacidosis is supportive with IV glucose and bicarbonate. Bicarbonate therapy is often required long term. While protein restriction is not usually necessary, protein rich diets and ketogenic diets should be avoided. Carnitine supplementation can be used. The family should monitor urinary ketones to be alert for impending metabolic crisis.
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. Despite severe recurrent attacks, appropriate supportive care can result in normal development.
Natural History with treatment:	With early diagnosis and treatment apparently normal development occurs.
Metabolic Information	
Missing Enzyme & Location:	Mitochondrial acetoacetyl-CoA thiolase enzyme- Normally interconverts 2-methylacetoacetyl-CoA to propionyl-CoA plus acetyl-CoA.
MS/MS profile:	C5:1 (tiglyl or 3-methylcrotonyl carnitine)- elevated. C5-OH (3-hydroxy-2-methylbutyryl carnitine) – elevated.
Prenatal testing:	Enzyme analysis on amniocytes or CVS is possible. If mutation is known, can perform mutation analysis.

Miscellaneous Information:	No phenotype/genotype correlation.	
Credit:	<i>Prepared by the North West Regional Newborn Screening Program Judith Tuerck, RN, MS, and Lorinda Paradise at Oregon Health Services University in Portland, Oregon and by Sara Copeland MD, Iowa Neonatal Metabolic Screening Program.</i>	
Sites of Reference:	OMIM - 3 Ketothiolase Deficiency (2-Methylacetoacetyl-CoA Thiolase) www.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?203750	
Support Groups:	Organic Acidemia Association www.oaanews.org/ 13210 35th Avenue Plymouth, MN 55441 Contact: Kathy Stagni (763) 559-1797 OAAnews@aol.com	