



Genetic Fact Sheets for Professionals

Fatty Acid Oxidation Disorders

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)

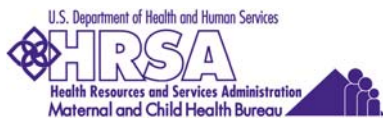
Disease name	Late-onset glutaric acidemia, type 2
Alternate name(s)	Glutaric aciduria, type II, Glutaric aciduria IIB, Glutaric aciduria IIC, Multiple acyl-CoA dehydrogenase deficiency, Ethylmalonic-adipidic aciduria, Electron transfer flavoprotein deficiency, Electron transfer flavoprotein dehydrogenase deficiency, ETFA deficiency, ETFB deficiency, ETFDH Deficiency
Acronym	GA2, GAI, MAD, MADD
Disease classification	Fatty Acid Oxidation Disorder Organic Acid Disorder
Inheritance	Autosomal recessive
Variants	Yes
Variant name	Glutaric acidemia type II (early onset)
Symptom onset	Late infancy, childhood and early adulthood
Symptoms	<p>There are three different phenotypes that stay consistent within families – neonatal onset with congenital abnormalities, neonatal onset without anomalies and mild or late onset disease. Phenotype is most likely related to the amount of residual enzyme activity. Those infants with the lowest residual enzyme activity are the most severely affected. Infants with higher residual enzyme activity are less severely affected.</p> <p>Neonatal onset with congenital anomalies: See GA2 factsheet</p> <p>Neonatal onset without anomalies: See GA2 factsheet</p> <p>Mild or late-onset GA2: Symptoms are very variable in course and age of presentation. They include episodes of hypoketotic hypoglycemia and hepatic dysfunction. There is progressive lipid storage myopathy and carnitine deficiency and a few individuals have had progressive extrapyramidal movement disorders similar to GA1. There are some reports of asymptomatic adults.</p>

Natural history without treatment	Variable depending on the age of presentation and severity of symptoms.
Natural history with treatment	For individuals with the milder late onset type, therapy may prevent some of the neurological findings and the carnitine deficiency.
Treatment	Treatment of the severe neonatal presentations is not effective (see GA2 fact sheet). The efficacy of treatment for late-onset glutaric acidemia, type 2 is unknown. Treatment can include the following: dietary restriction of fat and protein, riboflavin supplementation, carnitine supplementation and glycine supplementation.
Other	Sweaty foot odor has been reported. Urine organic acids may only be abnormal during acute episodes. Mothers have been reported with HELLP syndrome. Has been implicated as a cause of SIDS.
Physical phenotype	No obvious dysmorphisms have been reported. One infant presented with macrocephaly. Some individuals may present with cardiomegaly and cardiomyopathy.
Inheritance	Autosomal recessive
General population incidence	Unknown
Ethnic differences	None known
Population	N/A
Ethnic incidence	N/A
Enzyme location	Mitochondria
Enzyme function	Transport of electrons from the acyl-CoAs to ubiquinone (CoQ ₁₀) of the mitochondrial electron transport chain
Missing enzyme	ETFA – alpha subunit of electron transfer flavoprotein ETFB – beta subunit of electron transfer flavoprotein ETFDH – electron transfer flavoprotein dehydrogenase
Metabolite changes	Increased glutaric, lactic, ethylmalonic, butyric, isobutyric, 2-methylbutyric and isovaleric acids.
Gene	Three separate genes can cause the same disorder – ETFA, ETFB, and ETFDH. Individuals with late-onset glutaric acidemia, type 2 appear to have varying amounts of residual enzyme activity.

Gene location	ETFA – 15q23-q25 ETFB – 19q13.3 ETFDH – 4q32-qter
DNA testing available	No
DNA testing detail	N/A
Prenatal testing	Yes - analyte analysis of amniotic fluid or enzyme analysis of amniocytes.
MS/MS profile	C5DC - elevated C4; C5; C6; C8; C10 - multiple elevations C6 hexanoyl carnitine - mild elevations C8 octanoyl-carnitine - elevated C16; C18:1 - multiple elevations
OMIM link	www.ncbi.nlm.nih.gov/htbinpost/Omim/dispim?231680 www.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?608053 www.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?130410 www.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?231675
Genetests link	www.genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888891&fcn=c&qry=16897&res=nous&res=noinfl&key=yrzmfmrblDPma&show_flag=c
Support group	Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org
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