



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	Methylmalonic acidemia, Vitamin B-12 responsive
Alternate name(s)	Methylmalonic acidemia, Vitamin B-12 responsive, due to defect in adenosylcobalamin, cblA complementation type; Methylmalonic acidemia, cblA type; Methylmalonic acidemia, Vitamin B-12 responsive, due to defect in synthesis of adenosylcobalamin, cbl B complementation type
Acronym	MMA, MMAA/MMAB
Disease classification	Organic Acid Disorder
Inheritance	Autosomal recessive
Variants	Yes
Variant names	Methylmalonic acidemia, Vitamin B-12 non-responsive; Combined deficiency of methylmalonyl-CoA mutase and homocysteine
Symptom onset	Variable. Ranges from the first days of life to completely asymptomatic.
Symptoms	Episodic ketoacidosis with vomiting accompanied by lethargy and coma which can lead to death. Survivors can have developmental delays, growth retardation, spastic quadriparesis, dystonia and seizures. Neutropenia, thrombocytopenia and osteoporosis are common complications.
Natural history without treatment	Variable depending on the enzyme defect. Some will die in the newborn period, others will survive with deficits and others will be asymptomatic.
Natural history with treatment	CblA: Good prognosis with injections of hydroxycobalamin (OH-cbl) which reverses biochemical and clinical abnormalities in about 90% of patients.

CblB: Equal fractions of affected patients are alive and well, alive and impaired, or deceased. The age of onset of symptoms can help prognosticate outcome – those patients with a later onset of symptoms have a more benign course. Approximately 40% of patients will respond with a drop in MMA level when given OH-cbl injections.

Treatment	Protein restricted diet, OH-cbl injections, carnitine supplementation, oral antibiotic therapy to decrease proprionate and medical foods. Liver transplant or combined liver/kidney transplant may increase metabolic control, but may not prevent neurologic complications.
Other	N/A
Physical phenotype	Minor facial dysmorphisms including high forehead, broad nasal bridge, epicanthal folds, long, smooth philtrum and triangular mouth. A variety of skin lesions can be seen in patients due to moniliasis.
Inheritance	Autosomal recessive
General population incidence	1:48,000
Ethnic differences	No known population at increased risk
Population	N/A
Ethnic incidence	N/A
Enzyme location	Mitochondria
Enzyme function	Production of adenosylcobalamin
Missing enzyme	Cobalamin A (cblA) deficiency: cobalamin reductase Cobalamin B (cblB) deficiency: cobalamin adenosyltransferase
Metabolite changes	Elevated glycine in urine
Gene	MMAA (cobalamin A disease) MMAB (cobalamin B disease)
Gene location	MMAA: 4q31.1-q31.2 MMAB: 12q24

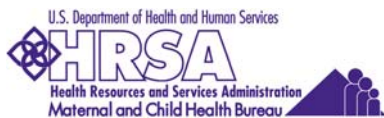
DNA testing available	Sequencing available internationally
DNA testing detail	N/A
Prenatal testing	Possible via enzyme assay on amniocytes or CVS
MS/MS profile	Elevated C3 propionyl carnitine, elevated C4 DC methylmalonyl carnitine.
OMIM link	www.ncbi.nlm.nih.gov/entrez/dispmim.cgi?id=251100
Genetests link	www.genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888891&fcn=c&qry=22174&res=nous&res=nointl&key=ya10OD5WOSqMG&show_flag=c
Support Group	Organic Acidemia Association www.oaanews.org
	Save Babies through Screening Foundation www.savebabies.org
	Genetic Alliance www.geneticalliance.org
	Fatty Oxidation Disorder (FOD) Family Support Group www.fodsupport.org
	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>