



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	Vitamin B12 metabolic defect with methylmalonic acidemia and homocystinuria
Alternate name(s)	Combined deficiency of methylmalonyl-CoA mutase and Homocysteine
Acronym	N/A
Disease classification	Organic Acid Disorder
Inheritance	Autosomal recessive
Variants	Yes
Variant name	Methylmalonic acidemia, Vitamin B-12 responsive, Methylmalonic acidemia, Vitamin B-12 non-responsive
Symptom onset	CblC has the earliest age of onset ranging from the first year of life to 14 years. Most patients described have been symptomatic from early in life.
Symptoms	CblC disease: Early onset patients may have feeding problems, hypotonia, failure to thrive, seizures, microcephaly, developmental delay, cortical atrophy, hydrocephalus, nystagmus, pigmentary retinopathy, decreased visual acuity and bone marrow dysfunction. Late-onset patients present in childhood or adolescence with acute neurological changes including decreased cognitive performance, confusion, dementia, delirium, myelopathy and tremor. Only one late-onset patient had pigmentary retinopathy. Hematological abnormalities may also be seen in late-onset patients. They may have progressive neurological deficits in spite of appropriate treatment.
Natural history without treatment	Clinical courses range from sudden death to severe psychosis and developmental delay.
Natural history with treatment	Early diagnosis and prompt institution of therapy may be the only way to change the outcome of these patients. Treatment thus far has not been successful. It is not clear that the treatment changes the natural history, but may help to decrease some of the psychiatric complications and

hopefully avoid some of the skin rashes and other secondary complications such as pigmentary retinopathy and renal involvement.

Treatment	Protein-restricted diet, OH-cbl supplementation, betaine treatment, carnitine supplementation.
Other	N/A
Physical phenotype	None special
Inheritance	Autosomal recessive
General population incidence	Unknown
Ethnic differences	None known
Population	N/A
Ethnic incidence	N/A
Enzyme location	CblC – precise defect not known
Enzyme function	CblC – precise defect not known
Missing enzyme	CblC – precise defect not known
Metabolite changes	Methylmalonic acid and homocysteine levels are elevated in blood and urine.
Gene	CblC
Gene location	All gene locations are unknown.
DNA testing available	No
DNA testing detail	N/A
Prenatal testing	Enzyme assay is available on CVS or amniocytes for known at-risk families.
MS/MS profile	Elevated C3 propionyl carnitine, elevated C4 DC methylmalonyl carnitine, low methionine .
OMIM link	CblC: www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=277400 CblD: www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=277410 CblF: www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=277380

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

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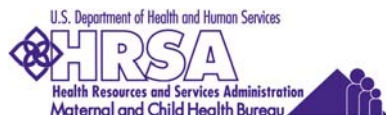
Reviewed by HI, CA, OR and WA metabolic specialists

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Update on N/A

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