

Disease Name	
3-METHYLGLUTACONIC ACIDURIA TYPE II (MGA II)	
<i>(X-LINKED CARIOSKELATAL MYOPATHY, NEUTROPENIA & ABNORMAL MITOCHONDRIA) (BARTH SYNDROME; MGA, TYPE II)</i>	
Classification:	Organic aciduria
Genetic Information	
Inheritance:	X-linked.
Population Incidence:	Rare, less than 50 cases described (probably under diagnosed).
Ethnic Incidence:	No known population at increased risk.
Gene & Location:	G4.5 protein (tafazzin) gene on Xq28
Common Mutation:	No known common mutations.
OMIM #	#302060; *300394
Disease Information	
Symptom Onset:	Presents in the neonatal period.
Symptoms:	The initial presentation of the syndrome varies. Newborns tend to be small for gestational age. Prenatal detection of cardiac abnormalities has been found in some affected infants. Dilated cardiomyopathy, cyclic neutropenia, growth retardation, short stature, skeletal myopathy and 3-methylglutaconic aciduria (3MGA) are the most common clinical findings. 3MGAuria is variable and tends to be less severe than that seen in MGA, Type 1. Shoulder and pelvic muscles are most affected by the skeletal myopathy and is progressive, while extraocular and bulbar muscles are spared. Neutropenia has been noted on cord blood studies, tends to be congenital but varies with time. Differentiation in bone marrow becomes arrested at the myelocyte stage causing granulocytopenia. Patients die from overwhelming infection or cardiac failure have been reports of sudden infant death, which may be related to arrhythmia. Common infections observed are bacterial skin lesions and oral aphthous lesions without severe illness. The cardiomyopathy and frequency and severity of bacterial infections decreased with age in some families. Over time the facial features become myopathic. Patients with Barth syndrome may have some specific learning problems. In one limited study, problems with visual-spatial learning and visual motor scores were noted. IQ does not appear to be much different from age matched controls. However, there was a tendency toward lower math scores.
Physical Findings:	No dysmorphisms, as they age tend to have myopathic appearance to their faces.
Treatment:	Carnitine does not appear to improve cardiac function; in one patient it caused heart failure. Some authors propose that it is contraindicated. Pantothenic acid, a precursor for coenzyme A, has been used in some with improved cardiac function. However, oral pantothenol not efficacious. Otherwise, there are no specific therapies available except supportive care for cardiac problems and infection. The cardiomyopathy responds to digoxin therapy and some patients have been placed on granulocyte colony stimulating factor (GCSF) for the neutropenia.
Natural History without treatment:	Without care of the neutropenia and cardiac failure patients will die.
Natural History with treatment:	If care is given, the patient has improved chance of survival but still at high risk for morbidity and mortality.
Metabolic Information	

Missing Enzyme & Location:	The basic enzyme defect involves cardiolipin, membrane lipid with importance to stability of mitochondrial respiratory chain.	
MS/MS profile:	C5-OH (3-hydroxyisovaleryl carnitine) - elevated	
Prenatal testing:	Possible if mutation previously identified in family.	
Miscellaneous Information:	In two families with documented G4.5 mutations, no 3-methylglutaconic acid has been found on analysis of urine organic acids.	
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 - Methylmalonic Aciduria www.ncbi.nlm.nih.gov/htbin-post/Omim/dispmim?251000	
Support Groups:	Organic Acidemia Association www.oaanews.org/ 13210 35th Avenue Plymouth, MN 55441 Contact: Kathy Stagni (763) 559-1797 OAANews@aol.com	The Barth Syndrome Foundation, Inc. P.O. Box 974 Perry, FL 32348 850-223-1128 Fax: 402-421-1926 inquiries.rd@barthsyndrome.org www.barthsyndrome.org