



Barth Syndrome FAQ's

- **What is Barth syndrome?**
 - Barth syndrome is a rare but serious, x-linked genetic disorder of lipid metabolism primarily affecting males around the world.
- **What are the signs and symptoms of Barth syndrome?**
 - The cardinal characteristics of this multi-system disorder consist of the following in varying degrees:
 - **Cardiomyopathy (dilated or hypertrophic)** - A weak heart muscle usually associated with enlargement of the heart
 - **Neutropenia (chronic, cyclic, or intermittent)** - A reduction in "neutrophils", a type of white blood cell that is most important for fighting bacterial infections.
 - **Muscle hypoplasia and weakness/Exercise intolerance** - All muscles, including the heart, have a cellular deficiency which limits their ability to produce energy. Muscle weakness and increased exertional fatigue are characteristic findings in Barth syndrome.
 - **Growth Delay** (often mistaken to be failure to thrive)-During childhood most affected individuals are below-average in height and weight.
 - **3 Methylglutaconic aciduria** - An increase in an organic acid that can be measured in urine that result in abnormal mitochondria function (the "powerhouses" or primary energy producers in cells).
 - **Cardiolipin deficiency** - A failure of Barth syndrome mitochondria to make adequate amounts of tetralinoleoyl-cardiolipin, an essential lipid (fat-like molecule) for normal mitochondrial structure and energy.
- **What gene is affected?**
 - Barth syndrome is caused by mutations in the tafazzin gene (*TAZ*, also called G4.5) on the X chromosome. Because males have only one X chromosome, they will have signs of Barth syndrome if that X chromosome carries a mutated tafazzin gene.
- **Who does Barth syndrome affect?**
 - Barth syndrome primarily affects males.
- **Can females get Barth syndrome?**
 - Females are primarily only carriers of the mutated gene that causes Barth syndrome. Females who carry an X chromosome with a tafazzin mutation are unaffected because they have a second X-chromosomes with a normal tafazzin gene that is dominant to the recessive tafazzin gene. Although it is theoretically possible for a female who carries a mutation in the Barth gene to have clinical signs of the disorder, there has been no proven affected female with a normal 46, XX female karyotype to date.
- **How does someone get Barth syndrome?**
 - Barth syndrome is an x-linked recessive genetic condition, meaning that it can be transferred from mother to son. A mother who is a carrier of Barth syndrome usually shows no signs or symptoms of the disorder herself. There is a 50% chance that a boy born to a female carrier will have Barth syndrome, while girls born to a carrier have a 50% chance of being carriers themselves. All daughters of a male with Barth syndrome will be carriers, though none of his sons will be affected. There are several known non-carrier mothers, and for this reason we believe mothers should be tested.
- **How is Barth syndrome diagnosed?** The diagnosis of Barth syndrome should be considered for any child or adult found to have any one of its four cardinal clinical characteristics, and evaluation for the other diagnostic criteria should be undertaken by obtaining the following studies:
 - Quantitative urine organic acid analysis, including quantification of 3-methylglutaconic acid
 - Cardiolipin analysis of muscle, platelets or cultured cells
 - Complete blood count and differential
 - Echocardiogram

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The Barth Syndrome Foundation www.barthsyndrome.org

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- DNA sequence analysis (genetic testing) of the tafazzin gene (TAZ, also called G4.5) which falls on the long q arm of the X chromosome; Xq28.
 - Please see the “Diagnosis of Barth syndrome” webpage for further information on diagnosing Barth syndrome as presented by Dr. Richard Kelly MD, Ph.D.
 - For more details about these tests and a listing of approved labs, please refer to <http://www.genetests.com>.
- **Why is an early diagnosis critical?**
 - Early and accurate diagnosis is key to survival for affected individuals. Historically, boys died of heart failure or infection by three years of age, but today, with improved diagnosis, treatment, and management, the survival rate and future of these boys is much brighter.
- **What are the major clinical problems?**
 - Congestive heart failure
 - Risk of serious arrhythmia, including sudden death
 - Serious bacterial infections
 - Gross motor and/or fine motor delay
 - Growth delay
 - Exercise intolerance, lack of stamina
- **Are there other possible clinical problems?**
 - Frequent diarrhea
 - Recurrent aphthous ulcers
 - Hypoglycemia, including fasting hypoglycemia in the newborn period
 - Osteoporosis
 - Chronic headache and body aches, especially during puberty
 - Extreme fatigue
 - Feeding problems
 - Mild learning disabilities
- **Incidence and Prevalence**
 - To date, there are no good studies of the population or birth incidence of Barth syndrome; however probably fewer than 10 new Barth infants are identified each year in the United States, which suggests an incidence of only 1 in every 300,000 – 400,000 births. Currently there are fewer than 500 individuals within our registry from around the world.
- **Ethnic Incidence**
 - Barth syndrome occurs in many different ethnic groups and does not appear to be more common or have originated in any one group.
- **When was Barth syndrome first described?**
 - Dr. Peter Barth of The Netherlands published the first comprehensive description of Barth syndrome in 1981 and again in 1983.
 - Dr. Richard Kelley at the Kennedy Krieger Institute at John Hopkins published a further study on Barth syndrome in 1991.
- **When was the Barth gene identified?**
 - In 1996, the specific genetic location of the Barth gene on the X-chromosome was identified. (Bione, et al 1996)
- **Is there a cure for Barth syndrome?**
 - There is no specific cure for Barth syndrome at this time, but the BSF is funding research for interested scientists and physicians in hopes to further their understanding of the metabolic and biochemical abnormalities seen in this disease.
- **How do you treat Barth syndrome?**
 - There are no specific treatments for Barth syndrome. Not all patients exhibit all of the symptoms at any one time, therefore heart symptoms, infections, and nutrition problems are treated as they arise. Careful attention and monitoring for symptoms is advised.