



Barth Syndrome Foundation

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The Barth Syndrome Foundation

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Barth syndrome ~

A Closer Look for Families



Barth Syndrome Foundation

Making a difference
in the lives of those
affected by
Barth syndrome

www.barthsyndrome.org

What is Barth syndrome?

Barth syndrome is a serious X-linked genetic disorder. The characteristics (signs and symptoms) consist of the following, in varying degrees:

Cardiomyopathy:

A weak heart muscle usually associated with enlargement of the heart (dilated or hypertrophic).

Neutropenia (cyclic, chronic or intermittent):

A reduction in “neutrophils”, a type of white blood cell that is most important for fighting bacterial infections. Neutropenia may predispose an individual to mouth ulcers, fevers and bacterial infections such as bacterial pneumonia and skin abscesses.

Muscle weakness:

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:

During childhood most affected individuals are below-average in height and weight. This is often assumed to be evidence of poor nutrition or other secondary effects of a chronic illness, but that is rarely the case. In fact, some of the common nutritional treatments are contra-indicated. Through BSF’s registry, we have observed accelerated growth to normal height during mid- to late- teenage years.

3-Methylglutaconic aciduria (an increase in an organic acid that can be measured in urine):

A result of abnormal mitochondria function. However, there have been reports of normal levels of 3-methylglutaconic acid in confirmed cases of Barth syndrome.

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 metabolism.

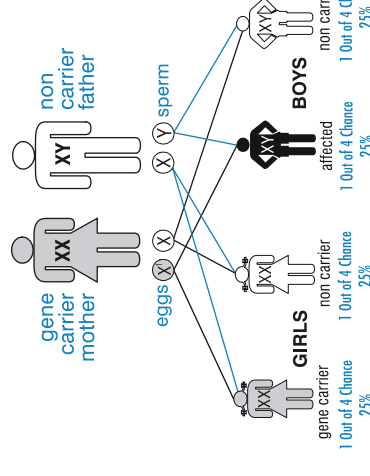
For more information about how a firm diagnosis can be achieved, please visit our website at:

www.barthsyndrome.org

Barth syndrome inheritance

Barth syndrome is an X-linked recessive genetic condition, generally transferred from mother to son. A mother who is a carrier of Barth syndrome 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% risk 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.



Highlights of Research

- 1981 *Barth et al.* first fully described "An X-linked & mitochondrial disease affecting cardiac muscle, skeletal muscle and neutrophil leucocytes."
- 1983 *Kelley et al.* found 3-methylglutaconic aciduria to be a biochemical marker for Barth syndrome.
- 1991 *Cox et al.* reported that G-CSF can be used successfully to treat Barth neutropenia.
- 1996 *Bione et al.* discovered the gene on distal arm of Xq28 [called *TAZ1* or *G4.5*; proteins encoded by the gene called tafazzin(s)].
- 1997 *Adwani et al.* documented heart transplantation as being successful in Barth patient.
- 1997 *Newald* hypothesized that tafazzin is an acyl-transferase involved in phospholipid biosynthesis.
- 1998 Shown by *Orstavik et al.* that female carriers of Barth syndrome are healthy due to extremely skewed pattern of X-chromosome inactivation.
- 2000 *Vreken et al.* demonstrated that tafazzin is involved in cardioliipin remodeling in Barth fibroblasts.
- 2001 *Mazzocco et al.* published preliminary data suggesting a cognitive phenotype for Barth syndrome, including some difficulties with math and tasks involving visual spatial abilities.
- 2002 *Schlarme et al.* found tetralinoleoyl-cardiolipin to be nearly absent in platelets, fibroblasts and muscle from Barth patients.
- 2003 *Greenberg et al.* constructed a *taz1* yeast mutant model.*
- 2004 *Strauss et al.* and *Degli Esposti et al.* independently created zebrafish knock-in models of Barth syndrome; *Strauss* demonstrated that the *G4.5* gene is essential for normal cardiac development in zebrafish.*
- 2004 *Gonzalez* presented data that only two functional forms of *G4.5* mRNA exist (delta 5 and full-length) in humans; also noted that exon 5 does not exist in yeast or rodents and that the full ability to splice developed only after evolutionary split from Old World monkeys, but is important to humans.*
- 2005 *Spencer et al.* documented the risk of serious arrhythmias and sudden cardiac death in adolescent Barth patients.*

Currently, *Drosophila* (a fruit fly) and mouse models of Barth syndrome are being developed.

* Research projects funded by BSF, Inc.

The Barth Syndrome Foundation

Members of the Foundation have access to the most current information as it relates to research and treatment of Barth syndrome.

BSF provides the following services:

- A friendly and supportive environment for families affected by Barth syndrome.
- Access to the latest research findings and treatment of Barth syndrome.
- Two issues of BSF'S Newsletter yearly
- An e-mail-based Listserv for families, the medical community and other professionals to exchange knowledgeable information about this complex disorder.
- An international medical conference every two years which brings together BSF affected families, the medical community and researchers to exchange information on Barth syndrome and to accelerate scientific and medical advances.
- The world's largest centralized registry of affected individuals.

We also actively work to:

- Promote awareness of Barth syndrome amongst the wider medical community and with families for early diagnosis.
- Raise funds to support research and our ongoing programs and activities.

Learn more at:

www.barthsyndrome.org



Your invitation — Join now

Join us today, at no cost:

- Twice yearly BSF Newsletter.
- Use of the BSF Listserv.
- Invitation to the multi-track, International Family and Scientific Conference every two years.
- Up-to-date information on latest treatment information and research findings.
- An opportunity to participate in BSF's International Medical Database.

Contact us at:

inquiries@barthsyndrome.org

We encourage you to contact us to discuss anything in this brochure or to learn more. Details of how to reach BSF and our affiliates are included on the back page. There is power in knowledge and strength in numbers; please get in touch with us.



"When I think of BSF I think of 'Hope'."

It is 'Hope' that gives me the strength and

endurance to fight!"

~ Casie Oldewage

Saving lives through education, advances in treatment and pursuit of a cure for Barth syndrome