



Barth Syndrome Trust

www.barthsyndrome.org.uk

What is Barth syndrome?

Barth syndrome (BTHS; OMIM 302060) is a rarely diagnosed genetic disorder that affects males. It is caused by a recessive X-linked defect in the tafazzin gene, resulting in an inborn error of metabolism.

The main symptoms of Barth syndrome include:

- **Cardiomyopathy**
dilated or hypertrophic sometimes with left ventricular non-compaction and/or endocardial fibroelastosis
- **Neutropaenia**
chronic, cyclic or intermittent
- **Skeletal myopathy**
with general fatigue
- **Growth delay**
that can be substantial until late teenage years

Please note that there is great variability between different patients. There is also great variability with regard to any single individual over time.

Cardiomyopathy and/or neutropaenia may not always be present at diagnosis and may vary with age.

Major clinical problems

- Congestive heart failure
- Gross motor delay
- Growth delay until late teenage years
- Exercise intolerance, lack of stamina
- Risk of serious bacterial infections
- Risk of fatal arrhythmia

Other clinical observations

- Foetal death / stillbirth
- Feeding problems
- Frequent diarrhoea
- Recurrent mouth ulcers
- Hypoglycaemia, especially during early childhood
- Characteristic facial appearance (large ears, deep set eyes, myopathic facies), nasal quality to speech, waddling gait, positive Gower's sign
- High incidence of minor congenital malformations
- Osteoporosis
- Chronic headache and body aches, especially during puberty
- Mild learning disabilities
- Cardiolipin abnormalities
- 3-methylglutaconic aciduria

Boys with Barth syndrome often look deceptively healthy



Photo by Amanda Clark

Diagnostic testing

- Cardiolipin analysis from a bloodspot on a Guthrie card
- DNA sequence analysis (genetic testing) of the tafazzin gene

Interesting observations

Incidence

So far, 11 living patients have been identified from 8 genetically distinct families in south west England and south Wales (population approximately 6 million). This suggests that there may be at least 110 cases in the UK. Most of these cases remain undiagnosed at present.

I'm quite sure it is under-diagnosed. If you've never heard of the disease, you're not going to look; you're not going to find.

Jeffrey Towbin, MD, Cincinnati Children's Hospital

Cardiac

Cardiomyopathy is usually dilated but can be hypertrophic. It can also oscillate between the two forms. Left ventricular non-compaction can occur.

Misdiagnosis

It is often misdiagnosed as viral myocarditis during infancy. This may be due in part to its sudden presentation at a time when neutropaenia, growth and muscle weakness may not yet be fully apparent.

Heart transplant

Severity may fluctuate dramatically and unpredictably. It is not unusual to see cases where patients have been considered for transplant, only to be taken off the transplant list when there is a sudden and dramatic improvement in cardiac function. However, function can deteriorate again and a transplant may become necessary in cases where medical therapy has been unsuccessful. Many boys have undergone successful transplantation and continue to do well years later.

Arrhythmia

There is a risk of arrhythmia and sudden cardiac death, even when heart function may be low-end normal.

Neutropaenia

The complexity and variability of this disorder often means that infections may be indolent and difficult to diagnose. When boys are well, the neutrophil count may approach zero, often only rising to normal or above during an acute infection. Many patients have benefited from G-CSF and/or prophylactic antibiotic therapy.

Metabolic issues

Severe hypoglycaemia can occur during short periods of fasting. Reduced muscle mass can cause increased muscle wasting with normal overnight fasting. Eating the correct amount of cornstarch before bed is often useful. Dehydration and electrolyte imbalances can develop quickly during periods of diarrhoea/vomiting and extra vigilance when giving IV fluids is advised.

Anaesthesia

Special consideration should be given to the selection of anaesthetic agents - please contact us for a copy of our guidelines.



Boys at a Barth syndrome clinic

Growth

Through BSF's registry, we have observed accelerated growth during late teenage years when boys reach or even exceed their predicted adult height (average shift from the 4th centile up to 16 years to 80th centile by the age of 19).

Phases of Barth syndrome

Children are often seriously ill before the age of 5 years. There is usually a marked improvement during mid-childhood (6-11years), the 'honeymoon phase'. Adolescence often signals another difficult period.

Barth Syndrome Trust

(affiliated to Barth Syndrome Foundation)

We are part of a worldwide community of medical professionals, scientists and affected families. We work together to raise awareness of the disorder, to provide a leading source of information on all aspects of Barth syndrome and to support research.

For families affected by Barth syndrome, we provide support through our Family Services team, information, access to experts and a private email forum. We have regular specialised clinics and family gatherings.

Please contact us to:

- Access information on symptoms, treatments and the latest research findings
- Access the world's largest reference source of published literature on Barth syndrome
- Interact with Barth syndrome experts worldwide via our private doctors' email forum
- Access up-to-date data from our registry of the world's largest group of individuals with Barth syndrome
- Receive our Newsletter
- Receive an invitation to our International Scientific/Medical and Family Conference

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Please consider this disease in any boy with cardiomyopathy of any form, muscle weakness, neutropaenia or hypoglycaemia, or in any family with a history of multiple male death in childhood.

Dr C. Steward, Paediatrician, Bristol Royal Hospital for Children

Useful contacts in UK

The Barth Syndrome Trust (UK and Europe)

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These consultants can all be contacted at:
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International Registry and DNA Bank Advisory Committee

www.peds.ufl.edu/barthsyndromeregistry

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Members:

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Useful contacts around the world

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