## Major clinical problems

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

## Other clinical features

- Fetal death / stillbirth / male miscarriages
- Feeding problems and savoury food fads
- Episodic diarrhoea
- Recurrent mouth ulcers
- Characteristic facial appearance (large ears, deep set eyes, chubby cheeks), 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 difficulties
- Cardiolipin abnormalities
- 3-methylglutaconic aciduria

Boys with Barth syndrome often look deceptively healthy


## Diagnostic testing

- Free cardiolipin analysis
- DNA sequence analysis (genetic testing) of the *TAZ* gene

# Interesting observations

## Incidence

Less than 200 cases of Barth syndrome have been diagnosed worldwide. However as at April 2012, there were 30 unrelated diagnosed families in the UK , with a staggering 75% of these in southern England alone. This implies a much higher frequency than previously thought.

## Cardiac issues

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

Around 70% of patients develop cardiomyopathy in the first year of life*.

### *Misdiagnosis*

It is often misdiagnosed as viral myocarditis during infancy.

### *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. Around 14% of all diagnosed cases require transplantation, with 80% occurring before the age of 5.*

### *Arrhythmia*

There is a risk of arrhythmia and sudden cardiac death, (20% in general but this rises to 43% in patients over 11 years of age*) even when heart function may be low-end normal.

## Neutropenia

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. See guidelines for night-time cornstarch regime. Dehydration and electrolyte imbalances can develop quickly during periods of diarrhoea or 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

We have observed accelerated growth during late teenage years when boys reach or even exceed their predicted adult height (average shift from the 4$^{th}$ centile up to 16 years to 80$^{th}$ 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.

* Statistics courtesy of Barth Syndrome Registry

# Barth Syndrome Trust

**Please contact us to:**

- Obtain a referral to the NHS Clinic
- 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

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

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


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## NHS Service—Important information for all patients and doctors

This service includes

- Diagnosis (at no cost to the patient)
- Initial patient assessment and advice
- Multidisciplinary clinics for UK and European patients
- Close liaison with local physicians

### Clinics

Annual clinics include in-depth investigation and consultations with the following teams: cardiology, haematology, genetics, dietetics, metabolism, gastroenterology, endocrinology, dentistry, physiotherapy, occupational therapy, psychology, clinical nurse specialist

### NHS Specialised Service

Bristol Royal Hospital for Children

### General Enquiries and Haematology

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Barth Syndrome Trust®

www.barthsyndrome.org.uk

# What is Barth syndrome?

Barth syndrome (BTHS; OMIM 302060) is a rarely diagnosed genetic disorder that primarily affects males. It is caused by a recessive X-linked defect in the *TAZ* (*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
- **Neutropenia**
  chronic, cyclic or intermittent BUT sometimes absent
- **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 as well as great variability with regard to any single individual over time.
Cardiomyopathy and/or neutropenia may not always be present at diagnosis and may vary with age.