University Hospitals Bristol NHS

NHS Foundation Trust

Bristol Royal Hospital for Children

a national centre of expertise for

Barth syndrome

Barth syndrome is a rarely diagnosed genetic disorder that primarily 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 and/or left ventricular non-compaction and/or endocardial fibroelastosis
- **Neutropaenia**
  chronic, cyclical or intermittent
  BUT some males are never neutropaenic
- **Delayed motor development,**
  myopathy and excessive fatigue
- **Growth delay**
  that can be substantial until late teens

Boys at a Barth syndrome clinic

There is great variability between different patients and in 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
- Risk of serious bacterial infections
- Motor delay and proximal myopathy
- Growth delay until late teenage years
- Exercise intolerance, lack of stamina
- Risk of fatal arrhythmia
- Hypoglycaemia and lactic acidosis

Other clinical features

- Male foetal hydrops or stillbirth
- Feeding problems and savoury food fads
- Episodic diarrhoea
- Recurrent mouth ulcers
- Characteristic facial appearance (large ears, deep set eyes), nasal quality to speech, waddling gait, positive Gower's sign
- Osteoporosis
- Chronic headache and body aches

Boys with Barth syndrome often look deceptively healthy

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

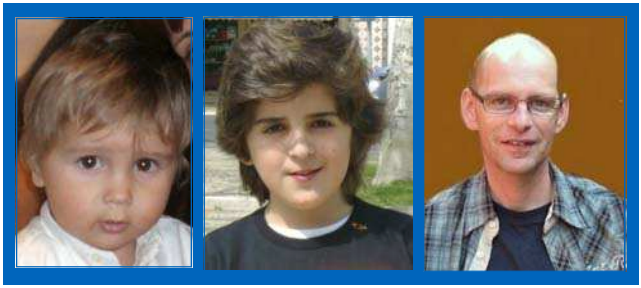
The NCG Barth Syndrome Service

New Nationally Commissioned Barth Syndrome Service from 1 April 2010

Important information for all patients and doctors

Working alongside local physicians, this is a national, multidisciplinary, patient-centred service run by a team who are experts in the condition. The service includes:

- Diagnosis — biochemical cardiolipin assay. (MLCL/CL ratio), confirmed by genetic testing where indicated
  MLCL/CL ratio is the only reliable diagnostic biochemical test
- Initial patient assessment and advice within 2 weeks of diagnosis
- A dedicated Clinical Nurse Specialist
- "One Stop" Clinic annually. The next Clinic will be held on 24-25th September 2010
- Close liaison with local physicians
- Retrospective analysis from Guthrie spots, stored DNA or cell lines for families with suspicious histories of male cardiac death, or families with histories of recurrent male foetal loss
- Referrals from EU countries provided that E112 is completed



The service will include expert assessment in the following areas:

Cardiology – detailed assessment of cardiac function including echocardiography, 12 lead ECG and 24-hour ECG, exercise testing etc

Haematology – assessment of possible neutropaenia, antibiotic prophylaxis, prescription of granulocyte colony stimulating factor (G-CSF), organisation of parental training on injection technique and home supply of the drug

Genetics – initial genetic counselling, antenatal testing (peripheral blood sample testing to determine sex of foetus, CVS, amnio etc)

Dietetics and metabolic issues – analysis of food diaries, advice regarding feeding problems, appropriate diets, anticipated growth rates, nasogastric and gastrostomy care, dietary adjustments to potentially alleviate symptoms

Gastroenterology – management of diarrhoea

Endocrinology – investigation into and management of delayed growth in childhood and accelerated growth after puberty

Physiotherapy and occupational therapy – assessment of muscle strength, exercise regimes to improve core stability and strength, orthotics

Psychology and Social Worker – to provide assessment and assistance in all related areas

Clinical Nurse Specialist – to ensure effective communication between all parties involved and to provide holistic and patient centred care of the highest standard. The CNS will visit affected families at home and school and will provide information and training in all matters pertaining to the proper management of Barth syndrome

Who should be referred for testing?

Any male infant, child or adult presenting with one or more of the following:

- Cardiac abnormality (dilated cardiomyopathy, left ventricular non-compaction cardiomyopathy)
- Unexplained intermittent, persistent or cyclical neutropaenia
- Unexplained hypoglycaemia and/or lactic acidosis
- Proximal myopathy
- Feeding difficulties and Failure to Thrive

Any female adult with a history of multiple still-births, foetal hydrops or foetal cardiomyopathy.

Please contact us for further details if you are

- a parent of a child with Barth syndrome or
- a doctor who would like to arrange a test for Barth syndrome or
- treating a patient who is eligible for referral to this service

Our address

Departments of Paediatric Haematology and/or Cardiology
Bristol Royal Hospital for Children
Paul O'Gorman Building
Upper Maudlin Street
Bristol
BS2 8BJ
barthsyndromeservice@uhbristol.nhs.uk

Useful contacts:

General Enquiries and Haematology

Colin G. Steward, FRCP, FRCPCH, PhD
Consultant Paediatrician
+44 (0)117 3428044

Cardiology

Beverly Tsai-Goodman, MD, MRCP
Consultant Paediatric and Foetal Cardiologist
+44 (0)117 3428856

Genetics

Ruth Newbury-Ecob, MD, FRCP, FRCPCH
Consultant Clinical Geneticist
+44 (0)117 9285107

These consultants can all be contacted at:
Bristol Royal Hospital for Children, Upper Maudlin Street, Bristol BS2 8BJ

The Barth Syndrome Trust (UK and Europe)

Michaela Damin, Chairperson
1 The Vikings, Romsey, Hampshire, SO51 5RG
Telephone: +44 (0)1794 518785
info@barthsyndrome.org.uk www.barthsyndrome.org.uk

International Registry and DNA Bank Advisory Committee

www.peds.ufl.edu/barthsyndromeregistry

Principal Investigators:

Carolyn Spencer, **MD**, Children's Hospital Boston
Barry J. Byrne, **MD**, **PhD**, Shands Children's Hospital, University of Florida

Members:

Richard I. Kelley, **MD**, **PhD**, Johns Hopkins University
Gerald F. Cox, **MD**, **PhD**, Children's Hospital Boston and Genzyme Corp.
Michael Schlame, **MD**, New York University School of Medicine
Colin G. Steward, **FRCP**, **FRCPCH**, **PhD**, Bristol Royal Hospital for Children
Matthew J. Toth, **PhD**, Barth Syndrome Foundation Science Director