E06/S(HSS)b

2013/14 NHS STANDARD CONTRACT
FOR BARTH SYNDROME SERVICE (CHILDREN)

PARTICULARS, SCHEDULE 2- THE SERVICES, A- SERVICE SPECIFICATIONS

Service Specification No.	E06/S(HSS)b
Service	Barth Syndrome Service (Children)
Commissioner Lead	
Provider Lead	
Period	12 months
Date of Review	

1. Population Needs

1.1 National/local context and evidence base

Barth Syndrome (BS) is rare metabolic disorder that most often occurs in males. A child with Barth Syndrome typically has these characteristics:

- heart muscle weakness;
- skeletal muscle abnormalities;
- low levels of white blood cells causing a condition called Neutropenia;
- slow development or weak muscle tone;
- increased levels of organic acids in the urine and blood;
- frequent bacterial infections, such as pneumonia.

1.2 Objectives and expected outcomes

Strategic service objective

To provide a holistic, patient centred service by a multi-disciplinary team.

The purposes and goals of the service

The service will:

- improve awareness, diagnosis and management of Barth Syndrome within the UK by education and provision of highly specific and sensitive diagnostic testing alongside liaison with and education of local healthcare providers;

- offer patient centred assessment and advice regarding the many organ

  specific problems associated with Barth Syndrome, with seamless transition into adult care;
- minimise impact on the patient and their family life, education and work practice;
- liaise with and advise healthcare workers in all relevant disciplines;
- enable consistent access to expert care across all relevant disciplines;
- provide patient specific cardiac assessment and management with close collaboration with local cardiologists;
- reduce the burden of hospital visits and inappropriate management for children and their families;
- ensure provision of blood specimens for validation of novel assays or research protocols (with patient consent);
- improve understanding of the unique patterns of neutropenia and related infection risk, and of variation in cardiomyopathy and arrhythmia risk.

1.2 Evidence base

First paper describing under-diagnosis of disorder & development of genetic testing in Bristol

Cantlay AM, Shokrollahi, K, Allen, JT, Lunt, PW, Newbury-Ecob RA, Steward CG. Genetic analysis of the G4.5 gene in families with suspected Barth Syndrome. J Ped 1999;135(3):311-5.

Development of reliable testing for Barth Syndrome

ulik W, van Lenthe H, Stet FS, Houtkooper RH, Kemp H, Stone JE, Steward CG, Wanders RJ, Vaz FM. Bloodspot assay using HPLC-tandem mass spectrometry for detection of Barth Syndrome. Clin Chem. 2008 Feb;54(2):371-8.

Description of a characteristic facial phenotype in Barth Syndrome

Hastings R, Steward CG, Tsai-Goodman B, Newbury-Ecob R. Dysmorpholgy of Barth Syndrome. Clin Dysmorphol. 2009 Oct;18(4):185-7

Cardiolipin and monolysocardiolipin analysis in fibroblasts, lymphocytes and tissues using HPLC-mass spectrometry as a diagnostic test for BS

Houtkooper RH, Rodenburg RJ, Thiels C, van Lenthe H, Stet F, Poll-The BT, Stone JE, Steward CG, Wanders RJ, Smeitink J, Kulik W and Vaz FM. Anal Biochem. 2009 Apr 15;387(2):230-7.

Cardiac and clinical phenotype in Barth Syndrome

Spencer, CT, Randall, MB, Day, J, Gonzalez, IL, Colan, SD, Reid Thompson, W, Berthy, J, Redfearn, SP, Byrne, BJ. Paediatrics, 2006 Aug: 118 (2): 337-346.

First Description of foetal death due to Barth Syndrome

Steward CG, Newbury-Ecob RA, Hastings R, Smithson SF, Tsai-Goodman B, Quarrell OW, Kulik W, Wanders R, Jones M, Williams M, JL Cresswell, Gonzalez IL, Brennan P. Barth Syndrome: An X-Linked Cause Of Foetal Cardiomyopathy And Stillbirth. . Prenatal Diagnosis 2010 Oct;30(10):970-6.

Other evidence includes:

Presentations to Royal College of Paediatrics and Child Health (RCPCH) Annual Meeting, American Societies of Haematology & Human Genetics. Invited lectures to

British Inherited Metabolic Disease Group, Clinical Genetics Society, Barth Syndrome Foundation meetings (including organisation of sessions) on incidence, cardiac presentation, dysmorphology, neutropenia & foetal loss. Paper in late stage draft on patterns and management of neutropenia in 60 worldwide BS patients.

2. Scope

Initial assessment:

This will entail an outpatient assessment for all new patients and will be offered within two weeks of diagnostic confirmation by cardiolipin analysis although the timing will depend on convenience for referring clinicians and families, fitness to travel and clinical need. Where patients have atypical components of presentation, confirmation by TAZ gene sequencing may be recommended first, with initial assessment offered within two weeks of receipt of that result.

Initial assessment will include cardiology investigations and haematology/biochemistry assessment, consultations with appropriately qualified and experienced designated consultants together with the clinical nurse specialist (CNS), genetic counsellor, dietician and psychologist. Consultations will also be organised with other subspecialists/Allied Health Professionals (AHP)s (metabolic, neurology, endocrine, speech and language, occupational therapy) where these are appropriate. From this will follow provision of detailed information and liaison with local paediatricians, haematologists, cardiologists, metabolic physicians, geneticists and dieticians as required.

On-going support provided:

Annual clinic assessments

Provision of the service will be through on-going support for patients, families and

clinicians as required, which will be coordinated primarily by the clinical nurse specialist. University Hospital Bristol (UHB) will provide an annual one-stop clinic for each patient. A subset of patients may be seen at six monthly intervals if they are

having particular problems. The clinic will be held over two days (usually a Thursday afternoon and Friday) so as to fit in with the social component of these clinics organised on Saturday by members of the Barth Syndrome Trust. This activity is spread over two days since fatigue is typically a major limiting feature of Barth Syndrome and therefore all of the patient care contacts necessary cannot occur in a single day without overtiring patients.

Adolescent and adult patients will be seen by the multi-disciplinary team, including where relevant, the following appropriately qualified and experienced designated staff:

- consultant cardiologist
- consultant haematologist
- clinical nurse specialist
- genetic counsellor
- dietician
- psychologist

Advice/liaison with local carers

After each clinic the multi-disciplinary team will liaise carefully by letter ± telephone with local carers, concentrating particularly on paediatric cardiologists, haematologists, general paediatricians and family practitioners. Further on-going advice is available from the service's website, and by email or telephone; full contact details are given on the relevant page of the Barth Syndrome Service website.

On-going outpatient support

Arrangements will be made for performance of a series of neutrophil counts via local hospital specialists or family practitioners. Antibiotic prophylaxis will be recommended in all patients found to be intermittently or persistently neutropenic. Therapy with granulocyte colony stimulating factor (G-CSF) will be recommended in those with severe neutropenia (absolute neutrophil count less than 0.5 $x10^9$/l) or in patients who are developing recurrent mouth ulcers, sore gums or other infections of probable neutropenic origin.

G-CSF is prescribed centrally at Bristol Royal Hospital for Children (BRHC) and distributed by courier via AAH Evolution Homecare. The service's clinical lead consultant and a pharmacist at (BRHC) are responsible for prescription of G-CSF and subsequent dose adjustment according to neutrophil counts and infection responses. A nurse will visit the patient's home, usually on three occasions, to give training in injection technique. Further visits may be offered occasionally where patients are particularly struggling or where training in fingerprick blood sampling is required in order to facilitate regular blood testing and appropriate provision of G-

CSF dosing. Additional support by telephone, e-mail or home visit is available from the CNS and clinical psychologist.

The service aims to develop a handheld record in order to optimise liaison between local carers and the Barth Syndrome team and specific training in fingerprick blood testing. Advice is given in conjunction with the Barth Syndrome Trust with regard to obtaining Disability Living Allowance, Carer's Allowance and other allowances to which patients/families might be entitled.

Inpatient care

There is a limited facility within the service for short periods of inpatient admission to try to allow more complex series of investigations, training or where patients are having complex and unexplained problems (especially where these require multidisciplinary investigation and assessment). Examples could include patients who are having major exacerbations of fatigue threatening their education, those in whom G-CSF control of neutropenia is proving difficult or where needle phobias are refractory to management in the home setting and are compromising G-CSF administration. This does not include a facility for routine management of cardiac care, treatment of infectious diseases or other general paediatric conditions not allied to Barth Syndrome.

Genetic counselling

This is offered at initial assessment since families often have major concern about other potential cases within their families and about carrier status. These consultations are often performed in conjunction with the consultant specialists allied to the service as understanding disease severity and therapeutic options may influence decisions about carrier testing, prenatal testing and termination of pregnancies. The important potential of early foetal sexing by peripheral blood testing is emphasised since this may minimise need for invasive testing by chorionic villus sampling (CVS) or amniocentesis.

There is careful liaison with local genetic services and information provision about cascade testing and antenatal diagnostic testing following identification of causative TAZ mutations.

The service is commissioned for all eligible patients from England and Scotland. The clinic can be accessed by any eligible patient who has been confirmed to have Barth Syndrome by positive MCLC/CL test irrespective of gender, age, sex, disability, religious belief. Interpreters or use of a language line will be provided for families for whom English is not their first language.

The service is expected to demonstrate equitable geographical access across the country and take actions to address gaps in access.

The provider will provide information to patients on public transport access and accommodation for patients and relatives as needed.

Close family members are encouraged to attend the clinic in order to follow a family-orientated approach.

An equality assessment impact has been completed for the establishment of this service

Referral criteria, sources and routes

Testing:

Samples for cardiolipin ratio testing would usually be received from members of cardiology, paediatric, haematology, genetics or pathology departments. More exceptionally they may be obtained via general practitioners. All specimens will only be accepted for testing provided they satisfy the criteria for testing.

Acceptance into the service: this occurs after positive cardiolipin testing (confirmed by the Biochemistry Laboratory at the Bristol Royal infirmary or the team of Dr Ron Wanders in Amsterdam). An abnormal result would usually be confirmed by finding of a TAZ gene mutation on genetic analysis.

Other patients:

Occasional adults may be accepted for general or specific advice where Barth Syndrome is being considered as a cause of previous foetal or sudden child death, or where biochemical or DNA analysis has returned indeterminate results. Such referrals would usually come via cardiologists, paediatricians or geneticists.

Genetic counselling or family members: carrier testing will be routinely offered to mothers of living or dead Barth Syndrome patients. If this proves to be positive, cascade testing will then be offered to women who may be carriers or to boys/men who could have Barth Syndrome. This will be organised either directly or via liaison with relevant genetics departments/consultants/counsellors.

Antenatal testing:

When pregnancy is reported in a known carrier female, we will advise foetal sexing by antenatal blood sampling. Where the pregnancy involves a male foetus, either chorionic villus sampling or amniocentesis can be offered by local obstetric departments. DNA mutation testing to exclude Barth Syndrome in the foetus will then be conducted at the Genetics Laboratory at Southmead Hospital, Bristol allied to the service.

Patients will have a proven positive MLCL/CL ratio before a referral will be accepted. Invitation will subsequently be sent for the annual Barth Syndrome clinic.

Exclusion criteria

Only patients who are shown not to have Barth Syndrome through biochemical and/or genetic testing will be excluded from this service.

3. Applicable Service Standards

3.1 Applicable national standards e.g. NICE, Royal College

The providers of the national EB service must ensure they are fully integrated into their trust's corporate and clinical governance arrangements and must comply fully with Clinical Negligence Scheme for Trusts (CNST) and Care Quality Commission (CQC) requirements in terms of quality and governance. The hub centres are responsible for overseeing the governance arrangement of any spoke clinic provided under sub-contractual arrangements.

Each centre will ensure that there are:

- regular meetings with patient representatives;
- all practitioners will participate in continuous professional development and networking;
- patient outcome data is recorded and audited across the service.

4. Key Service Outcomes

Outcomes

Age at Diagnosis

Improved access to diagnostic and familial genetic testing should lead to a downward shift in the average age at diagnosis. This in turn means that boys will start to benefit from improved management earlier in their lives.

Quality Performance Indicator	***Threshold***	***Method of measurement***	***Consequence of breach***	***Report Due***
Age at Diagnosis				
Age at Death				
Infections, Bacterial Infections, Non-cardiac Inpatient Stays				
Neutrophil Counts				
School Attendance				

5. Location of Provider Premises
University Hospitals Bristol NHS Foundation Trust