E. Pre-examination process

E1. Information for users and patients

Functional area: Biochemical Genetics

Introduction
The Biochemical Genetics service is comprised of two regional laboratories, screening and metabolic. The services provided by these laboratories are detailed below.

Biochemical Genetics is a subdivision of the Department of Specialised Laboratory Medicine, Leeds Teaching Hospitals Trust. It is located at the St James’s University Hospital site. Samples and mail for Biochemical Genetics should include reference to Block 46.

The laboratory is open from 08.30 to 17.00 Monday to Friday. There is no formal commitment to provide an analytical service outside these times, but this may be possible following prior discussion with the contacts listed below.

A map of the location of the department is available on request.

CPA Status: Accredited

Contacts:
Dr Mick Henderson, Consultant Clinical Scientist, Head of Service
0113 2066861
mick.henderson@nhs.net

Neonatal Screening
Screening Office, main enquiry service 0113 2065806

Miss Caroline Griffith, Principal Clinical Scientist 0113 2065087
caroline.griffith@nhs.net

Mr Timothy Williams, Laboratory and Clinical Systems Manager, 0113 2065806
timothy.williams2@nhs.net

Dr Michael Richards, Consultant Haematologist, Head of Haematology Screening Service, 0113 3928776.
Michael.richards8@nhs.net

Mrs Lisa Farrar, Antenatal & Newborn Haemoglobinopathy Screening Coordinator 0113 2065806
lisa.farrar@nhs.net

Antenatal Screening
Mr Daniel Herrera, Principal Clinical Scientist 0113 2066860
daniel.herrera@nhs.net
Neonatal Screening Service

Area Covered
This laboratory provides the neonatal screening service for all births in the following PCTs: North Yorkshire and York (except Hambleton/Richmondshire), Bradford and Airedale Teaching, Leeds, East Riding of Yorkshire, Hull Teaching, Calderdale, Kirklees and Wakefield.

Sample type
Heel prick bloodspots should be collected between day 5 and 7 onto the single leafed screening card supplied by Whatman, Schleicher and Schuell product no. 742777. They must be sent on the day of collection, by first class post, to the screening laboratory. We strongly recommend the use of the prepaid and pre-addressed screening envelopes produced to national design available from:

Nic Rosen Communications
86 Claremont Field
Ottery St Mary
EX11 1NP
01404 815 935

Analytical Programme
The profile of tests performed and the investigation and follow up protocols used by this laboratory adhere to national policy as defined by The UK Newborn Programme Centre: [https://www.gov.uk/topic/population-screening-programmes/newborn-blood-spot](https://www.gov.uk/topic/population-screening-programmes/newborn-blood-spot). In addition one metabolic condition with a high local prevalence is included in the profile.

All samples received are tested for phenylalanine (PKU), tyrosine and then succinyl acetone if tyrosine is raised (tyrosinaemia type 1), octanoyl carnitine (medium chain acyl CoA dehydrogenase deficiency), leucine (maple syrup urine disease), isovaleryl carnitine (isovaleric acidaemia), glutaryl carnitine (glutaric aciduria type 1), methionine (pyridoxine non-responsive homocystinuria), thyroid stimulating hormone (congenital hypothyroidism), immunoreactive trypsin (cystic fibrosis), and haemoglobin variants (sickle cell disease and thalassaemia).

For more information on the newer metabolic conditions see: [http://www.expandedscreening.org/site/home/start.asp](http://www.expandedscreening.org/site/home/start.asp)

Reporting of Results
All reports are sent as electronic messages via the CfH IT spine to Yorkshire CHRDs. Users of the service outside Yorkshire receive reports in paper format by first class post. CHRDs record the results and send a letter to the parent when they have a record that all screened conditions have been reported as ‘not suspected’.
Action is taken immediately on positive results according to national and locally agreed protocols. It is the policy of this laboratory to phone results to the relevant local paediatric consultant who will see the child quickly. An initial referral letter is sent in PDF format by NHS mail immediately to confirm the details of a positive result. It is followed by a further letter when confirmatory testing has been completed and this letter also confirms that the other screening tests have been performed.

Retention of Cards
Unused material remaining on the bloodspot cards are retained in a secure store for seven years. National policy recommends a minimum retention of five years. These cards may be made available for further clinical tests, but only after consultation between a requesting consultant paediatrician and the laboratory Director, and only with the written consent of the parent or a Court Order.

External Quality Assurance for bloodspot assays
NEQAS: Neonatal biochemical screening scheme, which includes phenylalanine, tyrosine, octanoylcarnitine (C8), decanoylcarnitine (C10), C8/C10 ratio, isovalerylcarnitine (C5), glutarylcarnitine (C5DC), leucine, methionine, TSH and IRT

Haemoglobin scheme

Down Syndrome TSH requests
The screening laboratory provides a service to facilitate regular monitoring of children with Downs syndrome for hypothyroidism. These children tend to have a phobia of needles making venepuncture difficult, but they are known to be at increased risk of developing hypothyroidism. TSH is measured in dried bloodspots. The cards sent to the laboratory must be clearly identified as ‘Downs TSH Monitoring’ and indicate the address for results to be reported. These cards must be filled out according to the pathology labelling policy to be accepted.

Antenatal Downs Screening Service
The screening laboratory provides biochemical analyses on blood samples taken during the first and second trimester of pregnancy and risk calculation for Down’s syndrome. Our screening service is commissioned to provide first trimester combined screening and second trimester screening in the form of triple or quadruple test. The reports generated are sent as PDF files by email to screening coordinators using secure NHS net accounts and contain a preformatted letter to patients. The laboratory provides specifically designed Antenatal Downs request cards. It is vital that these are completed fully and carefully, the information provided is essential for the risk calculation.

Collaboration with users of the screening services
There are multidisciplinary regional audit groups that meet twice a year to oversee the programme delivery of both neonatal and antenatal screening. These review current practice and ensure that the programmes meet current national standards. Minutes of these meetings are available on request.

Metabolic Laboratory Service

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Sample Type</th>
<th>Sample Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acylcarnitines</td>
<td>Bloodspots</td>
<td>Min 2 spots Mark bloodspot card to minimum standards of sample labelling and also send fully completed pathology request card.</td>
</tr>
<tr>
<td>Amino acids*</td>
<td>Plasma, lithium heparin</td>
<td>Min 200 µL (of plasma)</td>
</tr>
<tr>
<td>Amino acids*</td>
<td>Urine, plain container</td>
<td>Min 1.5 mL</td>
</tr>
<tr>
<td>Amino acids</td>
<td>CSF</td>
<td>Min 200 µL (send paired plasma sample)</td>
</tr>
<tr>
<td>Biotinidase</td>
<td>Serum</td>
<td>Min 200 µL (of serum) Separate sample asap (same day maximum), store and send frozen</td>
</tr>
<tr>
<td>Cystine, stone screen and cystinuria</td>
<td>Urine, acidified (pH&lt;2.0)</td>
<td>Aliquot from 24 hour collection or random sample (min 5.0mL)</td>
</tr>
<tr>
<td>Monitoring</td>
<td>Creatine and GAA (guanidinoacetic acid)</td>
<td>Urine, plain container &amp; lithium heparin plasma</td>
</tr>
<tr>
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<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Galactose-1-phosphate uridyl transferase</td>
<td>Whole blood, lithium heparin</td>
<td>Min 0.5mL. Invalid if baby recently transfused</td>
</tr>
<tr>
<td>Homocysteine, total</td>
<td>Plasma, EDTA</td>
<td>Min 0.5mL, separate within 30 min venepuncture</td>
</tr>
<tr>
<td>HVA, HMMA &amp; Dopamine</td>
<td>Spot urine, 25mL plain bottle containing 1.0mL 4M HCl</td>
<td>Min 5mL. Urine should be collected in the morning, before any meals but not the first sample passed after waking.</td>
</tr>
<tr>
<td>Lactate</td>
<td>Plasma, fluoride oxalate</td>
<td>Min 1.0 mL</td>
</tr>
<tr>
<td>Methylmalonic acid</td>
<td>Urine, plain container</td>
<td>Min 5 mL</td>
</tr>
<tr>
<td>Mucopolysaccharides</td>
<td>Urine, plain container</td>
<td>Min 3 mL</td>
</tr>
<tr>
<td>Oligosaccharides and sialic acids</td>
<td>Urine, plain container</td>
<td>Min 1.5 mL</td>
</tr>
<tr>
<td>Organic acids</td>
<td>Urine, plain container</td>
<td>Min 5 mL</td>
</tr>
<tr>
<td>Orotic acid</td>
<td>Urine, plain container</td>
<td>Min 2 mL</td>
</tr>
<tr>
<td>Sugars, mono and disaccharides</td>
<td>Urine, plain container</td>
<td>Min 0.5 mL</td>
</tr>
<tr>
<td>Sweat chloride</td>
<td>Sweat collected under controlled conditions following pilocarpine stimulation</td>
<td>By prior arrangement with the laboratory</td>
</tr>
<tr>
<td>White cell cystine</td>
<td>Whole blood, lithium heparin</td>
<td>Min 3 mL, to reach laboratory within 24 hrs of venepuncture (samples can only be accepted between 9am Monday to 14pm Fridays)</td>
</tr>
</tbody>
</table>

- Amino acid reports are provided as qualitative or quantitative depending on the nature of the request.
- Specific and rare amino acids can be requested, e.g. urine phosphoethanolamine, sulphocysteine

Use of the metabolic service
Samples sent on a routine basis for metabolic investigations are analysed and reported within one working week. Urgent analyses must be organised in advance by telephone to one of the points of contact listed.

No specific request cards are issued by the metabolic service due to the many different hospitals served. The only requirements are adequately completed cards and appropriately labelled samples.

Collaboration with users
There is a multidisciplinary metabolic team meeting which includes laboratory staff, dieticians, specialist nurses and the metabolic paediatricians. This group meets quarterly at St Luke’s Hospital Bradford to discuss the service and its provision and specific patient requirements. Records are kept of the attendance and action points but not the details of patients discussed.

External Quality Assurance
This laboratory has a strong record not only of participating in EQA but also being involved in its organisation.
Dr Mick Henderson is a Board member and Specialist Scientific Advisor to ERNDIM. Schemes that the laboratory participates in:

**ERNDIM, European:**
- Urine diagnostic proficiency (DPT) scheme
- Urine qualitative organic acids
- Urine mucopolysaccharides
- Plasma amino acids, quantitative
- Total homocysteine
- Bloodspot acylcarnitines
- Special assays in serum (SAS) - creatine, GAA, total homocysteine
- Special assays in urine (SAU) - creatine, GAA, creatinine, orotic acid

**NEQAS, Birmingham:**
- Quantitative phenylalanine (Phe, Tyr, Leu, Ileu, Val)
- Sweat testing
- Urinary Catecholamines (HVA, HMMA & Dopamine)

**Manchester, Willink:**
- Urine mucopolysaccharides

**CDC, Atlanta:**
- Acylcarnitines (quantitative), bloodspot phenylalanine and tyrosine (for PKU monitoring)
Costs
The current tariff is available on request from Dr Henderson

Investigation Guidelines
A useful set of investigation guidelines can be downloaded from the website of the MetBioNet at [www.metbio.net](http://www.metbio.net)

In addition to these the laboratory can provide copies of locally agreed protocols for investigating sudden unexpected death in infancy and acute metabolic emergencies.

Training and Education
The biochemical genetics laboratories are regarded as a regional training resource and welcome visits and periods of study by staff from other laboratories. Senior staff from the laboratories participate in and support a wide range of national and regional, multi-disciplinary, training and teaching programmes.