

Newborn Screening

Standard Operating Procedure

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Authors: Catherine Collingwood and Laura Kiely

Authorised By: Darren Powell

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1. General information

The newborn screening laboratory at Alder Hey, in line with the national Newborn Bloodspot Screening (NBS) programme, screens for 9 conditions selected on the basis that the benefits of screening outweigh the risks. Currently the conditions screened for are:

- Congenital Hypothyroidism (CHT)
- Cystic Fibrosis (CF)
- Sickle Cell disease (SCD) referred to as Haemoglobinopathies
- Six inherited metabolic diseases (IMDs). These are genetic diseases that affect the metabolism.
 - Phenylketonuria (PKU)
 - Medium-chain acyl-CoA dehydrogenase deficiency (MCADD)
 - Maple syrup urine disease (MSUD)
 - Isovaleric acidaemia (IVA)
 - Glutaric aciduria type 1 (GA1)
 - Homocystinuria (HCU)

On day 5 of life (or in exceptional circumstances between day 5 and day 8) a small amount of blood is collected from a heel prick and applied to a blood spot card. These samples are sent to our laboratory for testing.

Approximately 30000 newborn babies are screened each year at Alder Hey. The screening laboratory is closely aligned to the metabolic and routine sections within biochemistry. The metabolic section of the laboratory uses highly specialised biochemical techniques to aid diagnosis and management of inherited metabolic conditions, whilst the routine section supports the clinical specialties of Haematology, Endocrinology, Metabolic Medicine and Dietetic services within the hospital, enabling prompt confirmatory testing for all babies with presumptive positive screening results requiring follow up.

The laboratory is accredited to the internationally recognised UKAS ISO 15189:2012 standard for Medical laboratories.

Up to date information on newborn screening for patients and health care professionals is available via the website link below.

<https://www.gov.uk/guidance/newborn-blood-spot-screening-programme-overview>

2. Where to find us

Where to find us:



The entrance to the multi-story visitor car park is located off East Prescott Road.

The postal address for the laboratory is:

Newborn Screening Laboratory
Pathology Department
Alder Hey Children's Hospital
Eaton Road
Liverpool L12 2AP

Directions to Alder Hey can be found on the hospital website:

<https://alderhey.nhs.uk/parents-and-patients/before-you-visit/getting-to-alder-hey>

The laboratory is situated on the first floor of the Clinical Support block connected to the main hospital and highlighted above. External visitors to the laboratory should exit the atrium via the rotating doors next to WHSmith. The laboratory can be accessed via the doors on the right. Access is restricted but specimen reception staff can be contacted using the intercom. All visitors should report to the reception desk.

3. Laboratory Opening Hours

The Newborn Screening laboratory is open Monday to Friday 0900h – 1730h.

4. Key contacts

Newborn screening enquiries	0151 252 5489 screening.laboratory@nhs.net
Clinical advice (Director of Newborn Screening)	Dr Darren Powell 0151 252 5486 darren.powell@alderhey.nhs.uk
Clinical advice for Sickle Cell & Thalassaemia (Consultant Haematologist)	Dr Katherine Lindsay 0151 228 4811 Ext 3680 katherine.lindsay@alderhey.nhs.uk
Senior Biomedical Scientist	Paul Coakley 0151 252 5489 paul.coakley@alderhey.nhs.uk
Biomedical Scientists	Natalie Nugent / Beatrice Nambela
Data Administrator	Donna Morrison
Medical Laboratory Assistant	Katie Mullen

5. Making requests

Blood spot samples must be collected onto a completed newborn screening bloodspot card. The request *must* contain a minimum of the following information:

- Baby's NHS Number on a barcoded label
- Baby's name
- Baby's date of birth
- Gestational age
- Baby's weight
- Name of the person taking the sample
- Date sample taken

If information is missing, the sample will be rejected and a repeat requested

6. Sample collection

Samples for newborn screening should be collected on day 5 of life (where date of birth is day 0), unless there are exceptional circumstances.

Care should be taken to ensure that the filter paper card has not exceeded the expiry date printed. At least 4 blood spots, the size of the guide circles on the card, should be collected. See the [Newborn blood spot screening: sampling guidelines - GOV.UK \(www.gov.uk\)](https://www.gov.uk/newborn-blood-spot-screening-sampling-guidelines)

Samples with the following problems will be rejected as results may be unreliable and a repeat sample will be requested; collected <5 days of age, collected within 72 hours of a transfusion, insufficient sample (too small/blood not soaked through), incorrect blood application (multi-spotted/spotted both sides), compressed/damaged, possible faecal contamination (CF), missing/invalid NHS number, missing/invalid date of sample/date of birth, expired card, >14 days in transit or damaged in transit.

A repeat sample from the avoidable repeat category must be taken within three calendar days of receipt of request.

7. Transport of samples

Blood spot cards can be transported to the laboratory via courier or first class royal mail. Samples collected within Alder Hey can be transported via the pod system or delivered to the laboratory by hand. Samples should be dispatched on the day of collection or otherwise within 24 hours of sample collection. Dispatch should not be delayed in order to batch blood spot cards together for transport.

8. Protection of Personal Data and Information

Personal data and information on request forms is required in order for the laboratory to operate and may be stored on laboratory computer files. The intent of the laboratory is to ensure that any personal data and information is treated lawfully and in accordance with the NHS requirements concerning confidentiality and information security standards. To this end we fully endorse and adhere to the Trust Data Protection Policy, the requirements of which are primarily based upon the Data Protection Act 1998 which is the key piece of legislation covering security and confidentiality of personal information.

9. Newborn screening conditions

Congenital Hypothyroidism (CHT)

CHT has an incidence of approximately 1 in 3,000 births and occurs when a baby is born with an absence or reduced amount of active thyroid tissue, or a hormone synthesis enzyme defect. This results in a deficiency of the hormone produced by the thyroid (thyroxine or T4). Babies with CHT may show prolonged jaundice dry skin, coarse features, protruding tongue, slow feeding, bradycardia and constipation. If the condition is untreated physical and mental delay will usually follow. Treatment consists of replacing the thyroxine by an oral dose of this hormone in tablet form.

Some babies with CHT may not show any clinical symptoms but all will have a biochemical abnormality which can be detected by the laboratory screening test. Thyroid stimulating hormone (TSH) is raised in CHT and is the basis of the screening test. TSH is measured in a dried blood spot utilising a specific immunological method. Screening for this condition in the newborn was introduced at Alder Hey in 1981.

Cystic Fibrosis (CF)

Cystic Fibrosis affects 1 in 2500 babies born in the UK. In this condition there is a problem transporting chloride across cell membranes. This affects certain organs in the body, particularly the pancreas and lungs. In patients with Cystic Fibrosis, the thick secretions in these organs cause digestive problems and chest infections. The abnormal transport of chloride in sweat glands leads to an increased level of chloride in their sweat.

A number of studies suggest that children who are diagnosed following newborn screening might be healthier than those diagnosed later due to more timely treatments. Newborn screening for Cystic Fibrosis may also reduce any delays in diagnosis, reducing anxiety and uncertainty about why a child is ill. Early diagnosis of a baby with Cystic Fibrosis through newborn screening can also alert the parents to their risk of having other affected children. Biochemical screening for Cystic Fibrosis was introduced at Alder Hey in 2007 and uses a method to detect raised levels of immuno-reactive trypsinogen (IRT).

Sickle Cell disease (SCD)

About 1 in 2000 babies born in the UK has sickle cell disease. This is a serious inherited blood disease. Sickle cell disease affects the red blood cells, and babies with SCD require lifelong care. This screening test was first introduced at Alder Hey in 2004. The disorder is found mostly amongst people of African and Caribbean descent although it also occurs in other ethnic groups. Patients affected with the disease may experience painful or life-threatening crises and are often anaemic and jaundiced. The patients are prescribed life-long prophylactic antibiotics and are regularly followed up in our haemoglobinopathy clinic. Carriers for the disorder (sickle cell trait) are clinically well. Here at Alder Hey the screening test is performed using HPLC and confirmed using capillary electrophoresis.

Phenylketonuria (PKU)

PKU has an incidence of approximately 1 in 10,000 births. Screening for this disorder was introduced at Alder Hey in 1969. The disorder is inherited with both parents being asymptomatic carriers. Classical PKU is caused by a deficiency of the liver enzyme phenylalanine hydroxylase, which converts the amino acid phenylalanine to tyrosine. Phenylalanine accumulates in the baby's blood leading to brain damage. The high blood spot phenylalanine concentration is detected using tandem mass spectrometry. Following a screen positive, confirmatory diagnostic testing is undertaken.

Babies with PKU do not show any clinical signs at birth but without treatment those with the classical form of the disease become severely and irreversibly mentally handicapped. Treatment by restriction of the intake of dietary phenylalanine enables normal development.

Medium Chain Acyl CoA Dehydrogenase Deficiency (MCADD)

Approximately 1 in 10,000 babies born in the UK have MCADD. Babies with this inherited condition have problems breaking down fats at times of need, to make energy substrate for the body, in particular the brain. This can lead to serious illness, coma and even death. MCADD only causes problems when fats are need to be mobilised, for example if a baby has not eaten for a long period or if they have an infection, where requirement for energy is increased. Screening means that most babies who have MCADD can be recognised early in life, allowing special attention to be given to their diet, including making sure they eat regularly, and increase their intake of carbohydrates when unwell. This care can prevent serious illness and allow babies with MCADD to develop normally.

Screening for this is undertaken using tandem mass spectrometry and following a positive result further diagnostic testing is required to confirm the diagnosis, undertaken within the metabolic section of the laboratory.

Maple Syrup Urine Disease (MSUD)

Maple Syrup urine disease (MSUD) is a rare but treatable inherited disorder that prevents the normal breakdown of proteins. It has an incidence of 1 in 200000, is an enzyme defect that leads to a buildup of branch chain amino acids. These compounds can accumulate in tissues resulting in a life threatening metabolic event. The name of the condition derives from the sweet smelling urine sometimes produced in affected individuals, liked to the smell of maple syrup.

The classic form of this disorder presents shortly after birth, often in the first two weeks of life, hence early screening and identification is crucial. Symptoms include vomiting, difficulty with feeding, lethargy and neurological deterioration.

Screening for this is undertaken using tandem mass spectrometry and following a positive result further diagnostic testing is required to confirm the diagnosis, undertaken within the metabolic section of the laboratory. This was introduced in January 2015 as part of the expanded screening programme in the UK.

Isovaleric Acidaemia (IVA)

Isovaleric acidaemia is caused by a deficiency in an enzyme responsible for the breakdown of the amino acid leucine. It has an estimated incidence of 1 in 100000 although this can different in certain ethic groups. Due to the genetic diversity of this condition, the diseases can present in many ways. There is an acute neonatal form presenting characteristically within the first two weeks after birth. Symptoms include vomiting, lethargy, progressing to coma. Therefore early diagnosis is crucial to avoid the life threatening event.

Screening for this is undertaken using tandem mass spectrometry and following a positive result further diagnostic testing is required to confirm the diagnosis, undertaken within the metabolic section of the laboratory. This was introduced in January 2015 as part of the expanded screening programme in the UK.

Glutaric Aciduria Type 1 (GA1)

Glutaric aciduria is a condition caused by an enzyme deficiency with an estimated incidence of 1 in 100000. Defective breakdown causes toxic accumulation of glutaric acid leading to an encephalopathic crisis, most common around 9 months of age and most before 2 years, causing neurological deficit. Crisis occurs 1-3 days following a non-specific inter current illness, gastrointestinal infection or pneumonia, leading to dystonia and dyskinesia as permanent features.

Screening for this is undertaken using tandem mass spectrometry and following a positive result further diagnostic testing is required to confirm the diagnosis, some of which is undertaken within the metabolic section of the laboratory. Genetic studies may be required. This was introduced in January 2015 as part of the expanded screening programme in the UK.

Homocystinuria (HCU)

Homocystinuria is a defect in the enzyme cystathionine b synthase, referred to as “classical” HCU. It has an incidence in the UK of 1 in 100000. Children with this condition generally in the absence of screening would not be diagnosed until 2-3 years of age. Myopia followed by dislocation of the lens, osteoporosis, thinning and lengthening of the long bones, mental retardation and thromboembolism are the main features.

Screening for this is undertaken using tandem mass spectrometry and following a positive result further diagnostic testing is required to confirm the diagnosis, undertaken within the metabolic section of the laboratory. This was introduced in January 2015 as part of the expanded screening programme in the UK.

Hereditary tyrosinaemia type 1 (HT1)

Hereditary tyrosinaemia type 1 (HT1) Hereditary tyrosinaemia type 1 (HT1) is an autosomal recessive genetic disorder caused by deficiency of the enzyme fumarylacetoacetase (FAH). FAH catalyses the final step in the tyrosine degradation pathway, and when this enzyme is deficient there is accumulation of fumarylacetoacetate as well as of succinylacetoacetate and succinylacetone. These metabolites, particularly succinylacetone, cause hepatocellular damage and also result in the inhibition of other hepatic enzymes leading to elevated plasma tyrosine and delta-aminolevulinic acid (d-ALA). This in turn reduces haem synthesis and may cause porphyria-like acute neurologic episodes.

The birth incidence of HT1 is around 1:100,000 globally, and it is anticipated that newborn screening in the UK will detect around seven cases per annum.

The major clinical features of HT1 include severe liver disease manifesting as acute liver failure, coagulopathy, or chronic liver disease with the risk of hepatocellular carcinoma; renal tubular dysfunction, growth failure, and rickets; and neurologic crises, associated with neuropathic pain, acute mental disturbance, peripheral neuropathy and respiratory failure. Death occurs in untreated patients due to liver failure, neurologic crisis or hepatocellular carcinoma. HT1 can present in early infancy with acute liver failure but may also present later in infancy with growth failure and rickets being common presenting features.

Specific treatment for HT1 entails the use of nitisinone (NTBC) which inhibits the tyrosine degradation pathway before succinylacetoacetate and succinylacetone are generated and prevents the accumulation of these pathogenic metabolites. A tyrosine-restricted diet is also required to avoid hypertyrosinaemia from developing

secondary to the nitisinone blocking tyrosine degradation. Nitisinone and tyrosine-restricted diet can prevent the long-term complications of HT1 from developing.

Newborn screening for HT1 is based on the detection of elevated succinylacetone levels in the dried blood spot sample. Confirmatory testing uses a combination of biochemical and molecular genetic tests to establish a diagnosis of HT1.

Succinylacetone can also be elevated in patients who have deficiency of a different enzyme, maleylacetoacetate isomerase (MAAI), however MAAI deficiency is not associated with liver dysfunction or other long-term sequelae. The succinylacetone levels in MAAI deficiency are significantly lower than in HT1, and the confirmatory protocol is designed to differentiate these two disorders.

10. Suggestions and complaints

In order to improve the service you receive from the Newborn Screening laboratory, it is helpful to us if you keep us informed of any laboratory-related issues that you encounter. We aim to provide the very best service, but unfortunately we may not always get it right and sometimes things go wrong. It is important that we are informed about problems with our service as soon as possible. As the user of the service, you may be able to offer suggestions about our procedures, or changes in practice which may be helpful to you. Please contact the laboratory as soon as an issue is identified.

Regular User Group meetings for laboratory users within the Trust and for GPs are held to ensure that the requirements of users of our service are met by obtaining feedback and recommendations on quality improvements. For details of the User Group meetings please contact Julie Roberts (julie.roberts@alderhey.nhs.uk).

Patient queries and concerns can be addressed via the Trust Patient Advice Liaison Forum (PALS pals@alderhey.nhs.uk, 0151 252 5374).

Formal complaints can be made via the Trust Complaints Service (complaints@alderhey.nhs.uk).

Wherever possible the matter will be dealt with on the same day but not all issues can be resolved immediately, and some may be more serious or require a longer period of investigation and assessment within the department. Details of all complaints are recorded and reviewed at our monthly Leadership Team Quality and Governance Committee meetings. If a written complaint is received, a written reply will be provided.

11. Alder Hey Newborn Screening processes

An outline of the relevant processes together with reference to the relevant local standard operating procedures (SOPs) is shown in the organogram below.

1. Documentation

All laboratory documentation stored using the iPassport document control system. Each document is assigned a unique reference number.

2. Notification of samples unsuitable for analysis

Sample acceptance criteria are defined by the PHE Guidelines for Newborn Blood Spot Sampling ([Newborn Screening 1420](#)). The relevant midwifery office is informed by telephone if a blood spot repeat sample is required for any reason. Images of blood spot cards that are unsuitable for analysis are also sent to the relevant midwifery office via email.

3. Reporting of results and use of the Failsafe system

Receipt of blood spot cards and outcome e.g. “repeat required” or screening results e.g. “not suspected” are reported to the [Child Health Information System](#) (CHIS) via the Newborn Screening Failsafe system (NBSFS). Babies with “suspected” results are referred as required to the appropriate clinical team.

4. Performance standards

The laboratory policies, SOPs and target turnaround times are underpinned by the NHS Newborn Blood Spot Screening Programme Standards ([Biochemistry 1701](#)). Performance data is reported quarterly to the Cheshire and Mersey Antenatal Neonatal Newborn Screening Quality Assurance (QA) team and is submitted annually to the UK Newborn Screening Programme Centre.

Sample Reception	•Newborn Screening Specimen Reception Process •Process for Registering a Blood Spot Card in Newborn Screening •Process for dealing with 'Out of Area' Newborn Screening Reports •Newborn Screening Rejects Process •Declined testing in Newborn Screening	Newborn Screening 1276 Newborn Screening 1283 2 Newborn Screening 1337 Newborn Screening 1402 Newborn Screening 1278
Blood spot preparation	•Batch Creation and Worksheet Production Process •Preparation of Newborn Screening samples Using the Panthera Puncher	Newborn Screening 1296 2 Newborn Screening 1329
Blood spot analysis	•Newborn Screening for Congenital Hypothyroidism (CHT) •Newborn Screening for Cystic Fibrosis •Newborn Screening for Inherited Metabolic Disorders (PKU, MCADD, MSUD, IVA and GA1) •Newborn Screening for Sickle Cell Disease (HBOS) •Process for Dealing with SCID Testing in a non-SCID Screening Laboratory	Newborn Screening 1294 Newborn Screening 1296 Newborn Screening 1291 2 Newborn Screening 1285 Newborn Screening 2216
Reporting of Newborn Screening results	•Process for Checking Newborn Screening Cards (clearing) •Newborn Bloodspot Failsafe Solution Process	Newborn Screening 1286 Newborn Screening 1280
Supporting documents	•Procedure for Communication with Other Services in the Newborn Bloodspot Screening Pathway •Newborn Screening Service Continuity Plan •Newborn Screening Risk Management Policy •Newborn Screening Laboratory Handbook	Newborn Screening 2212 Newborn Screening 2209 Newborn Screening 2213 Newborn Screening 4971