Newborn blood spot sampling

Newborn blood spot screening should be offered to every newborn baby resident in the UK, and those that move into the UK up to the age of one year. Newborn blood spot screening tests are performed between 5-8 days after birth, ideally on day 5 (counting the date of birth as day 0). Blood spot sampling guidelines have been developed to provide a consistent approach to newborn blood spot sampling, reduce pain during the heel puncture and enable health professionals to obtain good quality samples and reduce the need for repeat samples.

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Key points

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1. All newborn babies should be offered newborn blood spot screening between 5-8 days after birth.
2. Babies admitted to NICU at less than five days of age should have a blood spot sample taken for sickle cell disease screening prior to transfusion, where possible.
3. Repeat blood spot samples should be taken at the equivalent of 36 weeks' (35 weeks + 7 days) gestation for congenital hypothyroidism.

Rationale for screening

Raffle and Gray[1] define screening as

> 'the testing of people without signs or symptoms of the condition being tested for, with the purpose of reducing the risk of ill health in relation to the condition being tested, or giving them information about the risk'.

Screening tests are never 100% sensitive[2]. Babies who are thought to be at higher risk of a condition are referred on for further tests and a definitive diagnosis. Appropriate diagnostic and treatment services must be in place for babies who screen positive[1]. Reports of delay in the initiation of treatment are widespread[3,4]; protocols must ensure timely access to the appropriate specialist and the healthcare professional must be familiar with all the steps in the screening programme so that prompt and relevant referrals can be made. The National Screening Committee (NSC) set criteria for appraising the viability, effectiveness and appropriateness of a screening programme[5].

Consent

Informed choice is a central part of healthcare policy in the UK[6-8] and is essential in gaining consent[9-10]. The healthcare practitioner is responsible for gaining consent prior to performing the screening procedures and must be able to communicate clearly with the baby's parents. Although newborn screening tests are recommended, parents have the choice to accept or decline screening.

All information for parents should be in a form that is accessible, taking into account any additional needs such as physical, cognitive or sensory disabilities and people who do not speak or read English[11]. It should be provided in the antenatal period and immediately before the test[12].

Newborn blood spot screening

Newborn blood spot screening identifies babies who may have rare but serious conditions. The NSC recommend that all babies in the UK are offered screening for phenylketonuria (PKU), congenital hypothyroidism, (CHT), sickle cell disease (SCD), cystic fibrosis (CF) and medium-chain acyl-CoA dehydrogenase deficiency (MCADD).

Newborn blood spot screening tests are performed on dried blood spot specimens collected on a specially designed blood spot card. The blood is collected from the baby's heel between 5-8 days after birth, ideally on day 5 (counting the date of birth as day 0).

The healthcare practitioner caring for the baby on day 5 is responsible for ensuring that the newborn blood spot screening is performed and sent off to the laboratory.

Phenylketonuria (PKU)

PKU has an incidence of 1 in 10,000 babies. It is an autosomal recessive genetic condition, caused by a deficiency of a liver enzyme called phenylalanine hydroxylase, which is necessary to break down phenylalanine, an amino acid present in many foods. If left untreated it almost always leads to severe mental disability as well as seizures. Effective therapy to lower raised blood phenylalanine levels by

dietary restriction of phenylalanine prevents progressive, irreversible cognitive damage but does not reverse pre-existing damage, and so the earlier treatment is commenced the better the ultimate outcome[13]. Babies who screen positive for PKU should be referred for treatment by 21 days of age[14].

It is possible for mothers to breast feed their babies with PKU so long as they balance the amount of breast milk with the baby's special dietary supplement. This may require mothers to express and discard their breast milk initially, until their baby's phenylalanine levels are within target levels[14].

Congenital hypothyroidism (CHT)

CHT is an autosomal recessive condition with an incidence of 1 in 4,000 babies and is more common in girls than boys with a ratio of 2.3 girls to every boy[14]. The majority of cases of CHT are sporadic with a low risk of recurrence in subsequent pregnancies.

In CHT the thyroid gland fails to function normally and a deficiency in the hormone thyroxine results. Babies who screen positive for CHT should be referred for treatment by 21 days of age[14]. If babies with CHT are not treated, they fail to grow properly and will have 'mild to severe' mental disability. In the most severe cases children also have a lack of co-ordination, jerky movements and tremors. In general, patients with complete absence of the thyroid gland (called thyroid agenesis) are the most severely affected. Treatment is by replacing thyroxine with a dose taken by mouth.

Cystic fibrosis (CF)

CF has an incidence of 1 in 2,500 babies. In CF there is a problem transporting chloride across cell membranes. This affects certain organs in the body, particularly the pancreas and lungs. The thick secretions in these organs cause digestive problems and chest infections. Cystic fibrosis can affect the baby before birth. Fifteen per cent of affected babies are born with blocked intestines, a condition called meconium ileus.

Treatment of children with CF aims to improve nutrition by providing supplements containing enzymes to help digestion; and reduce chest infections with frequent physiotherapy and either occasional or continuous antibiotics.

Sickle cell disease (SCD)

SCDs are rare autosomal recessive genetic diseases that affect the haemoglobin in the red cells. Incidence is 1 in 2,400 babies. Sickle cell affects the normal oxygen carrying capacity and when cells are de-oxygenated and under stress they can take on a sickle shape, become stiff and then get stuck in small blood vessels. This means the oxygen in the blood is unable to reach parts of the body. As a result people can experience very severe pain known as a 'crisis'.

If the test comes back positive the management of SCD is based on routine prophylactic penicillin for infants and the early use of antibiotics to prevent overwhelming infection. Babies should commence antibiotics by the time they are three months old[15].

Medium-chain acyl-CoA dehydrogenase deficiency (MCADD)

MCADD is a rare autosomal recessive genetic condition affecting 1 in 10,000-20,000 babies born in the UK[13]. MCADD occurs when the enzyme called medium-chain acyl-CoA dehydrogenase is either missing, or not functioning properly. This enzyme breaks down fats from food and from within the body, to convert into energy. Babies affected by MCADD often do not show any symptoms immediately after birth, but symptoms usually occur following a period of fasting or infection, for example if the child feels unwell and does not want to eat, or vomits[16]. Symptoms of MCADD can be highly variable but may include drowsiness or lethargy, diarrhoea, vomiting or fits. The baby may go into a coma called a 'metabolic crisis'. The primary focus of treatment is to avoid low blood sugar. Identifying newborns affected by MCADD allows parents to manage their baby's diet and ensure a regular, adequate energy intake for their child, thereby reducing the chances of severe, life-threatening episodes of illness. Parents are taught an emergency regimen to be used if the baby is unwell or not feeding. Glucose polymer feeds are given to provide energy[17]. Babies who screen positive should be referred to a specialist metabolic paediatrician by day 21.

Blood spot sampling guidelines

The aim of the guidelines is to achieve early detection, referral and treatment of babies thought to be affected by the various conditions described. The guidelines are designed to support health professionals in gaining consent for the blood spot test and to encourage the uptake of newborn blood spot screening through evidence-based information. The guidance aims to provide a consistent approach to newborn blood spot sampling, reduce pain during the heel puncture and enable health professionals to obtain good quality samples and reduce the need for repeat samples.

Preparation

It is important to offer parents an informed choice about screening for their baby, to gain consent and to prepare them for the blood sampling procedure. The booklet *Screening tests for you and your baby* is given to all pregnant women at the booking appointment. Healthcare professionals should discuss newborn screening in the third trimester of pregnancy and at least 24 hours pre-test[18-20]. A full explanation of blood spot screening should be given to parents.

The offer and acceptance or refusal of screening should be recorded in the maternity and/or baby notes and personal child health record (PCHR). Verbal consent is adequate and does not have to be signed by the parent(s). If parents decline all or part of the screening tests offered, a completed card marked DECLINE must be sent to the screening laboratory to monitor coverage of screening. The health professional must inform the general practitioner (GP) and health visitor (HV) of the conditions for which the baby has not been screened so that if symptoms arise they do not rule out the possibility of an affected child. If a parent does not wish to be contacted about future research on newborn blood spot screening, 'No research contact' should be recorded clearly on the card.

If the parents consent to screening, the blood spot sample should be taken on day 5 and certainly between day 5 and day 8 for all babies, regardless of milk feeding and prematurity. For the purpose of screening date of birth is counted as day 0.

Performing the blood spot sample

All fields on the blood spot card must be complete. Standard 2 of the UK Newborn Screening Programme Centre's Standards and Guidelines[21] recommends the use of a bar-coded babies' NHS number label. Where this is available the label should be

applied to the card and the other fields manually filled out. When completing the card care must be taken to avoid contamination through placing the card on a dirty surface or through touch. Care must be taken to confirm the baby's NHS number, name, date of birth and parents' contact details to ensure the correct label/information is recorded on the card. All relevant antenatal screening results must be recorded on the card, eg carrier of haemoglobin variants.

Comfort measures are recommended to reduce the pain during blood sampling in infants[22]. The baby should be cuddled in a secure position and engaging the baby through face-to-face contact, voice and touch may be beneficial[22]. Analgesia in the form of breast feeding, non-nutritive sucking and a dose of sucrose or glucose is beneficial[22,23]. Breast milk or breast feeding should always be preferred and sucrose used for situations where the mum or breast milk are not available[23].

To prevent contamination of the sample clean the heel by washing thoroughly with plain water or disinfecting with an alcohol swab for 30 seconds allowing the heel to completely dry before taking the sample. Faeces contain very high concentrations of immuno reactin trypsinogin (IRT). If the foot is not properly cleaned contamination with faeces can produce a raised IRT result. Obviously hands should be washed and gloves applied as a universal precaution before blood sampling.

The heel should be warm, but additional pre-warming of the foot is not required[24]. An automated lancet device designed for use on newborns should be used[24-28]. There is some evidence that an arc-shaped incision device is effective in providing a quality sample, reducing the number of heel puncture sites per test, the time taken to complete the test, the need for squeezing the heel, bruising, the time the baby cried, and the need to repeat the test[24].

Healthcare professionals must be instructed on how to use the device. Manual lancets *must not* be used. The external and internal limits of the calcaneus are the preferred puncture site marked by the shaded areas in **FIGURE 1A**. Skin puncture must be no deeper than 2.0 mm. There is some evidence that the whole of the plantar surface is safe for obtaining blood in term and preterm infants[29], marked by the shaded areas in **FIGURE 2B**. An automated lancet device designed for newborns with a penetrative

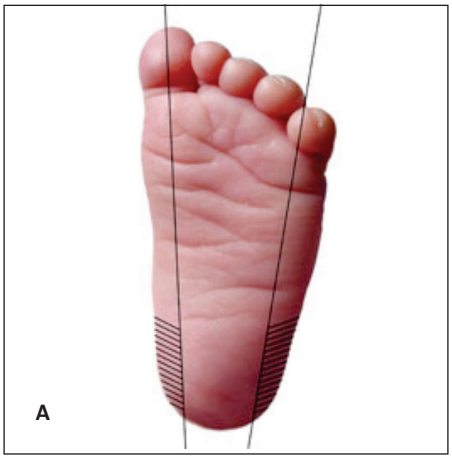

FIGURE 1 **A** - Preferred puncture site – the external and internal limits of the calcaneus. **B** - Possible puncture site for term and preterm infants – the whole of the plantar surface. Adapted from Jain and Rutter (1999). [30]

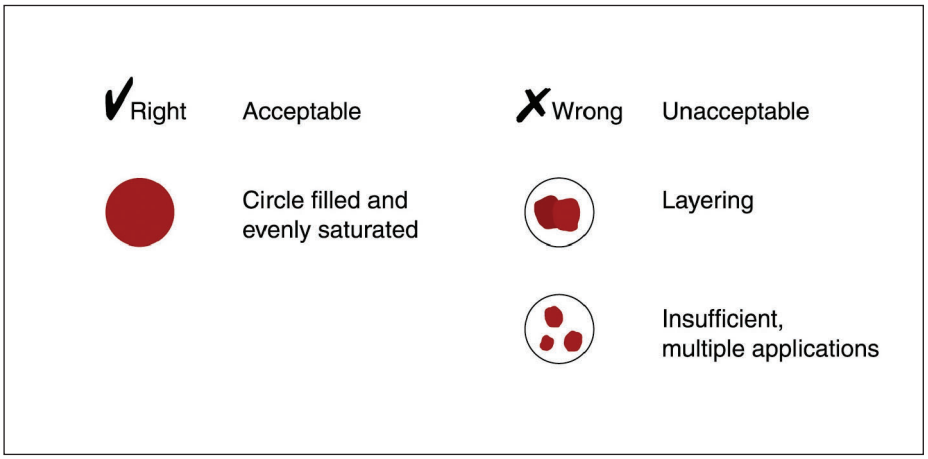

FIGURE 2 Acceptable and unacceptable examples of blood spotting.

depth of no more than 1.0 mm is recommended for preterm infants and when using the whole of the plantar surface. The posterior curvature of the heel must be avoided to minimise the risk of calcaneal puncture that may lead to calcaneal osteomyelitis (inflammation of the heel bone)[25-31].

Allow the foot to hang down to increase blood flow. Before activation place the automated lancet device against the heel in accordance with manufacturers' instructions. The aim is to fill the circles on the newborn blood spot card completely (**FIGURE 2**). Wait up to 15 seconds to allow blood to flow then allow one spot of blood to drop into each of the circles on the card. Fill the circle by natural flow, allowing the blood to seep through to the back of the card and avoid layering blood. Wipe excess blood from the heel and apply gentle pressure to the wound with cotton wool or gauze.

If the blood flow ceases, the congealed blood should be wiped away firmly with cotton wool or gauze. Gently 'massage' the foot, avoiding squeezing, and drop the blood onto the card. If the baby is not bleeding then a second puncture is necessary, this should be performed from a different part of the same foot or the other foot. Apply a spot plaster if required.

After taking the blood sample

It is important that the laboratory receives the blood sample promptly to ensure that babies who test positively are referred to the relevant specialist team and treatment is started where indicated. Parents also need to know when to expect the results. This will help reduce their concerns about the results, as well as providing an additional safety net in following up missing results.

Allow the blood spots to air-dry away from direct sunlight or heat before placing in the glassine envelope. Despatch the blood spot card within 24 hours of taking the sample and record date and method of sample despatch. Record taking the test in the mother's maternity record and PCHR. Record and notify screening status on

discharge/transfer and inform parents how and when they will receive results.

Special circumstances

This refers to babies nursed in neonatal intensive care units (NICU), born preterm and those who experience multiple blood spot samples taken from the heel. An assessment of the baby's level of distress and ability to tolerate handling must be made before initiating the comfort measures[32] described earlier in the article.

Babies admitted to NICU are likely to have multiple blood samples taken. Venepuncture or venous/arterial sampling from an existing line is an alternative, provided the sample is not contaminated with heparin and the line is cleared of infusate.

Ensuring coverage of newborn screening

Where possible blood spots should be taken for SCD screening prior to transfusion. Babies admitted to NICU at less than five days of age should have a single blood spot sample taken and marked as 'PRE-TRANSFUSION'. The 'PRE-TRANSFUSION' blood spot card should be stored with the baby's medical records and despatched to the newborn screening laboratory, with the day 5-8 sample if the baby has received a blood transfusion in the interim. All fields on both cards must be completed.

Where a baby has already had a blood transfusion either intrauterine or in the newborn period, before the screening blood sample is taken, repeat samples are needed 72 hours after the blood transfusion for PKU, CHT, CF and MCADD as well as at four months after the last blood transfusion for SCD (for intrauterine infusion count date of birth as date of transfusion)[33]. The date of the last blood transfusion must be recorded on the blood spot card. In the event of multiple transfusions an initial screening sample should be sent on day 8 regardless. Record the date and time of the last blood transfusion on the blood spot card and baby's discharge records. The parents should be informed that newborn screening is not completed, and the tests that are outstanding recorded and made obvious in the medical records, PCHR and transfer/discharge letters.

A repeat blood spot should be taken at the equivalent of 36 weeks (35 weeks + 7 days) gestation for CHT. It is recommended that there is a one week interval between repeat samples. The card should be marked 'repeat TSH' and care should be taken to make sure that gestation is recorded in weeks and days. A baby born at 34+6 weeks' gestation can have screening delayed until day 8 (between sampling range of 5-8 days).

Trusts should ensure failsafe arrangements for notifying screening status when the care of babies is transferred. This includes babies who are transferred in the neonatal period or discharged home before screening for all tests is complete.

The health visitor is responsible for ensuring that parents receive results and they are recorded in the PCHR.

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