Public Health England

NHS

NHS Newborn Blood Spot Screening Programme

Managing positive results from cystic fibrosis screening

Public Health England leads the NHS Screening Programmes

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-class science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health, and are a distinct delivery organisation with operational autonomy to advise and support government, local authorities and the NHS in a professionally independent manner.

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About PHE Screening

Screening identifies apparently healthy people who may be at increased risk of a disease or condition, enabling earlier treatment or better informed decisions. National population screening programmes are implemented in the NHS on the advice of the UK National Screening Committee (UK NSC), which makes independent, evidence-based recommendations to ministers in the 4 UK countries. The Screening Quality Assurance Service ensures programmes are safe and effective by checking that national standards are met. PHE leads the NHS Screening Programmes and hosts the UK NSC secretariat.

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Introduction

The NHS Newborn Blood Spot (NBS) Screening Programme aims to refer all screen-positive babies to diagnostic and clinical care in line with national guidelines and standards.[1] This document presents the recommended guidelines for managing positive results from cystic fibrosis (CF) NBS screening.

Part 1 presents guidelines for managing babies that have a screening result of 'CF suspected'. It also presents guidelines for 'probable carrier, low likelihood of CF' or 'CF not suspected' results following a second blood spot taken after an inconclusive result on the first sample.

Part 2 provides guidance on evaluating and managing infants with an unclear diagnosis after CF NBS screening – 'CF screen positive, inconclusive diagnosis (CFSPID)' cases.[2,3]

Links to supporting letter templates, resources and references are available throughout the document.

1. Processing positive results from CF newborn blood spot screening

a) Two *CFTR* mutations detected on the first blood spot sample – CF suspected

The responsibilities of agencies involved with the CF programme	
Screening laboratory	Refer the baby immediately to a designated person, or deputy, at the Regional CF Centre. This is the Centre that covers the baby's address on the blood spot card. Report the result by phone and in writing to the Regional CF Centre (use template letter). The screening laboratory should send a letter (use template letter) to the baby's GP informing them of the positive screening result. It is imperative that the GP understands that the result has been communicated directly to the Regional CF Centre who will make contact with the family. The letter is for information only.
Regional CF Centre (and network CF clinics)	Process the result promptly (perform the diagnostic assessment within **five working days** of receiving the result). In some circumstances, contact a local CF clinic if the clinic can provide the appropriate clinical and sweat test expertise (see later section). A local CF clinic is a recognised smaller clinic that works as part of a network with the Regional CF Centre at the hub of that network. The Regional CF Centre should contact the baby's primary care team (including their GP) to: • inform them of the screening result and plan contact with the family to give the result • ask if there are any relevant circumstances to be aware of • arrange a joint visit if possible
Primary care	The GP should contact the Regional CF Centre if they have concerns about the family or queries about the screening result.

team	
Interaction with the family (giving the NBS screening result)	
Models	There are a number of effective models for giving the screening result to the family. To some degree these models depend on local healthcare resources and organisations. Regardless of the model adopted, several evidence-based principles should be applied (see below).
Contacting family	Unless the primary care team has significant concerns, only inform the family of a positive screening result on a Monday, Tuesday or Wednesday. This avoids the diagnostic assessment being undertaken on a Friday or the family waiting over a weekend for the assessment. Inform the family by phone that the result will be discussed later that day. This enables the family to organise for more than one family member to be present. This should be an initial structured phone call by a healthcare professional with appropriate experience and support to give bad news. The positive CF screening result is usually given at a home visit but sometimes a second structured phone call alone is used. In both cases this should be undertaken by a healthcare professional with knowledge of screening and CF (CF clinical nurse specialist, screening link health visitor, screening nurse specialist or paediatrician). In all cases, a joint visit with the family health visitor with both parents present is optimal[4]. Give the parents the following resources and information: • 'Cystic fibrosis is suspected' leaflet • time and location of the diagnostic assessment for the following day • 'The sweat test' factsheet (available on the CF Trust website) Give the result to the family in the afternoon and offer parents/carers an appointment for the diagnostic assessment with the CF team the following morning. At this first encounter with the family, emphasise that this is a positive CF **screening** result and that diagnostic tests are needed for confirmation. Only give the family contact details given about the appointment.

Diagnostic assessment visit	
Where the assessment should take place	The diagnostic assessment should be undertaken by the CF team in a Regional CF Centre. In some circumstances the assessment may be undertaken in a CF clinic (a smaller network clinic that partners the Regional CF Centre). The CF clinic must have a team with the necessary experience to make and give a diagnosis, including an accredited sweat test service.
Investigations and clinical assessment	A sweat test is essential and should occur at the diagnostic assessment visit. Give the result of the sweat test to the family as soon as it is available (preferably on the same day). If a sweat test is not undertaken at the diagnostic assessment, or insufficient sweat is collected, organise repeat *CFTR* gene analysis at the diagnostic assessment. This can be undertaken on a blood sample or buccal (mouth) swab. A sweat test is required for all infants and this should include measurement of sweat chloride[5]. If unsuccessful at the first visit, repeat the sweat test at a later stage. The diagnostic assessment should include a clinical assessment of the infant. If concerned about progress, start appropriate treatment even if sweat test or confirmatory genetic results do not confirm the diagnosis at that point. Infants in this situation have a “presumptive” diagnosis of CF. Organise definitive confirmation of the diagnosis for these infants at the next clinical visit (within two weeks).
Early management and reporting	
Early management and reporting outcomes	At the initial discussion, explain the NBS screening programme and the genetic nature of CF to parents/carers. Also give a basic explanation of how CF is likely to affect the baby. It may not be appropriate for the family to spend time with all members of the CF team at the diagnostic assessment visit. Arrange for the CF team to visit the family over the next few days, or for the family to return to the Regional CF Centre/CF clinic.

	A CF nurse specialist should be available to give advice and support to the parents. Give the parents written information about CF (including a link to the CF Trust's new parent information pack). Introduce treatment regimens in a stepwise and timely manner, as deemed appropriate by the CF team. If the baby has respiratory symptoms or malnutrition or if there is family anxiety, it may be appropriate to admit the baby to initiate treatment more promptly. Communicate the outcome of the first appointment and diagnostic tests to the newborn screening laboratory, GP and family health visitor. Complete and return the 'Cystic fibrosis screening: CF suspected follow-up form' to the newborn screening laboratory within **24 hours** of assessment. The data in the form will be de-identified and reported to the NHS Newborn Blood Spot Screening Programme (Public Health England) as part of the annual data collection process to enable programme evaluation. For infants with a presumptive CF diagnosis, it is essential to forward the results of definitive testing to the laboratory, who in turn will update the NHS Newborn Blood Spot Screening Programme. Explore the benefits of, and encourage, registration of the baby on the UK CF Registry (with the parents' written consent).

b) One *CFTR* mutation detected and raised second IRT – CF suspected

Treat babies with this screening result as in part a) with the following consideration:

Interaction with the family (giving the NBS screening result)	
Contacting family	The family will have raised anxiety levels because a second blood spot sample has been collected. They should have been told the reason for the repeat and when to expect the result. Information on the second blood spot sample is available for healthcare professionals and parents. Inform the family of the CF suspected result promptly. Ideally this is within **24 hours** of the laboratory obtaining the second IRT result if the diagnostic appointment can be arranged for the next day.

c) No *CFTR* mutation detected but very high (≥ 99.9th centile) first IRT and raised second IRT – CF suspected

Treat babies with this screening result as in part a) with the following consideration:

Interaction with the family (giving the NBS screening result)	
Contacting family	The family will have raised anxiety levels because a second blood spot sample has been collected. They should have been told the reason for the repeat and when to expect the result. Information on the second blood spot sample is available for healthcare professionals and parents. Inform the family of the CF suspected result promptly. Ideally this is within **24 hours** of the laboratory obtaining the second IRT result if the diagnostic appointment can be arranged for the next day.

d) One *CFTR* mutation detected and normal second IRT – probable carrier, low likelihood of CF

Interaction with the family (giving the NBS screening result)	
Contacting family	The family will have raised anxiety levels because a second blood spot sample has been collected. They should have been told the reason for the repeat and when to expect the result. Information on the second blood spot sample is available for healthcare professionals and parents.

	Inform the family of the CF suspected result promptly. Ideally this is within **24 hours** of the laboratory obtaining the second IRT result.
Screening laboratory to family/designated health visitor	Where possible, the screening laboratory will have a screening nurse specialist who will contact the family health visitor (or preferably a designated health visitor if there is an appointed lead health visitor for giving screening results to families) by phone and confirm in writing.
Screening laboratory to GP	Inform the baby's GP of the result in writing. A template letter is available. Give the GP the 'Your baby carries the cystic fibrosis gene' leaflet and tell them which healthcare professional has been informed of the final result in order for this to be communicated to the parents.
Home visit and further support	
Home visit	The designated health visitor or alternate (who must be trained for the purpose) will visit the family to inform them of the result and give them the 'Your baby carries the cystic fibrosis gene' leaflet.
Further support	If the GP or family are concerned about a possible diagnosis of CF, the GP should refer the baby to a Regional CF Centre for further assessment. If the family is concerned about the genetic implications of the result, they should discuss this with their GP. If necessary the GP should refer the family to a clinical genetics centre. If the GP or family are concerned that the baby has symptoms of CF (poor weight gain, recurrent chest infections, rectal prolapse, nasal polyps), the baby should be referred to a Regional CF Centre.
Follow up	
Reporting outcome	The healthcare professional that gives the carrier result to the family should complete and return the 'Cystic fibrosis screening: carrier of CF gene follow-up form' to the newborn screening laboratory within **24 hours** of the visit. The data in the form will be de-identified and reported to the NHS Newborn Blood Spot Screening Programme as part of the annual data collection process to enable programme evaluation.

e) No *CFTR* mutation detected, very high first IRT (≥ 99.9th centile) but normal second IRT – CF not suspected

Interaction with the family (delivering the NBS screening result)	
Contacting family	The family are likely to have raised anxiety levels because a second blood spot sample has been collected. They should have been told the reason for the repeat and when to expect the result. Information on the second blood spot sample is available for healthcare professionals and parents. Inform the family of the CF not suspected result promptly. Ideally this is within **24 hours** of the laboratory obtaining the second IRT result.
Screening laboratory to family health visitor or midwife	Where possible, the newborn screening laboratory will have a screening nurse specialist who will contact the family health visitor or midwife by phone and confirm in writing. The family health visitor or midwife will contact the family to inform them of the result.

2. Evaluation and management of babies with an unclear diagnosis after CF newborn blood spot screening

a) Cystic fibrosis screen positive, inconclusive diagnosis (CFSPID)

These are babies with either:

- a normal sweat chloride (<30 mmol/L) and two *CFTR* mutations, at least one of which has unclear phenotypic consequences or
- an intermediate sweat chloride (30–59 mmol/L) and one or no *CFTR* mutations

Diagnosis	
Confirmatory diagnostic tests	Babies with an unclear diagnosis after CF newborn screening are designated as CF screen positive, inconclusive diagnosis (CFSPID).[3] These babies require further diagnostic assessment.[2] A Regional CF Centre should be involved in this assessment.[2] Undertake subsequent sweat testing in an accredited laboratory with considerable experience of this procedure.[2]
After the diagnosis	Manage babies with a CFSPID designation as per the European CF Society (ECFS) guidance.[3]
Follow up	
Reporting outcome	Communicate the outcome of the first appointment and diagnostic tests to the newborn screening laboratory, GP and family health visitor. Complete and return the 'Cystic fibrosis screening: CF suspected follow-up form' to the newborn screening laboratory **as soon as follow-up results are available**. The data in the form will be de-identified and reported to the NHS Newborn Blood Spot Screening Programme as part of the annual data collection process to enable programme evaluation.

Supporting information and letter templates

Taking a second blood spot sample for CF screening

- Information for healthcare professionals
- Information for parents

Managing 'CF suspected' screening results

- Template for notifying designated clinician (screening laboratory to clinician)
- Template for notifying GP (screening laboratory to GP)
- 'Cystic fibrosis is suspected' leaflet
- Follow-up form (clinician to screening laboratory)

Managing 'probable carrier, low likelihood of CF' results

- Template for notifying GP (screening laboratory to GP)
- 'Your baby carries the cystic fibrosis gene' leaflet
- Follow-up form (clinician to screening laboratory)

References

1. NHS England (2017) *NHS public health functions agreement 2017-18 Service specification no.19 NHS Newborn Blood Spot Screening Programme* [Online] Available at: www.england.nhs.uk/commissioning/pub-hlth-res/ (accessed: 05 May 2017).

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5. Guidelines Development Group (2014) *Guidelines for the Performance of the Sweat Test for the Investigation of Cystic Fibrosis in the UK 2nd Version: An Evidence Based Guideline* [Online] Available at: www.rcpch.ac.uk/improving-child-health/clinical-guidelines-and-standards/endorsed-and-supported/inherited-metabolic (accessed 05 May 2017).

Appendix 1: Communicating screening results to parents: CF is suspected (two mutations detected on first blood spot sample)

These guidelines support health professionals to communicate screening results to parents when cystic fibrosis (CF) is suspected (two mutations detected on first blood spot sample).

Guidelines for communicating CF suspected screening result	**Reasoning**	**Communication should include the following information**
The Regional CF Centre (or local CF clinic if applicable) should contact the baby's primary care team (including their GP) to: • inform them of the screening result and plan contact with the family to give the result • ask if there are any relevant circumstances to be aware of • arrange a joint visit if possible	The primary care team (including the family health visitor) has an ongoing role in supporting families.	
Unless the primary care team has significant concerns, only inform the family of a positive screening result on a Monday, Tuesday or Wednesday.	This avoids the diagnostic assessment being undertaken on a Friday or the family waiting over a weekend for the assessment.	
Inform the family by phone that the result will be discussed later that day. This should be an initial structured phone call by a healthcare professional with appropriate experience and support to give bad news.	This enables the family to organise for more than one family member to be present.	

The positive CF screening result is usually given at a home visit but sometimes a second structured phone call alone is used. In both cases this should be undertaken by a healthcare professional with knowledge of screening and CF (CF clinical nurse specialist, screening link health visitor, screening nurse specialist or paediatrician). In all cases, a joint visit with the family health visitor with both parents present is optimal.	A well-informed health professional should give information about CF suspected to parents.	Their baby's screening result suggests they may be affected by CF. Their baby will need further tests to confirm this result. Their baby does not need any urgent treatment now; they will receive advice about treatment from the specialist CF team over the next few days.
Give the parents the following resources and information: • 'Cystic fibrosis is suspected' leaflet • time and location of the diagnostic assessment for the following day • 'The sweat test' factsheet (available on the CF Trust website)	Parents will have questions about their baby's results. Parents can quickly forget or misunderstand the information they are given about their baby's results. They may also require access to reliable sources of further information and support.	The time and place of the appointment to see the specialist team and the name of the consultant. They will be able to discuss the screening result and treatment for their baby with the specialist CF team. Where they can get further information and support.
Give the result to the family in the afternoon and offer parents/carers an appointment for the diagnostic assessment with the CF team the following morning.	Delays in confirming results and starting treatment can only add to parents' anxiety.	
Record the result in the personal child health record and in the baby's notes.	Other healthcare professionals have access to the results.	

Appendix 2: Communicating screening results to parents: CF is suspected (one or no mutations detected on second IRT)

These guidelines support health professionals to communicate screening results to parents when cystic fibrosis (CF) is suspected (one or no mutations detected on second IRT).

Guidelines for communicating CF suspected screening result	**Reasoning**	**Communication should include the following information**
The Regional CF Centre (or local CF clinic if applicable) should contact the baby's primary care team (including their GP) to: • inform them of the screening result and plan contact with the family to give the result • ask if there are any relevant circumstances to be aware of • arrange a joint visit if possible	The primary care team (including the family health visitor) has an ongoing role in supporting families.	
Inform the family of the CF suspected result promptly. Ideally this is within **24 hours** of the laboratory obtaining the second IRT result if the diagnostic appointment can be arranged for the next day.	The family will have raised anxiety levels because a second blood spot sample has been collected. They should have been told the reason for the repeat and when to expect the result. Information on the second blood spot sample is available for healthcare professionals and parents.	

Inform the family by phone that the result will be discussed later that day. This should be an initial structured phone call by a healthcare professional with appropriate experience and support to give bad news.	This enables the family to organise for more than one family member to be present.	
The positive CF screening result is usually given at a home visit but sometimes a second structured phone call alone is used. In both cases this should be undertaken by a healthcare professional with knowledge of screening and CF (CF clinical nurse specialist, screening link health visitor, screening nurse specialist or paediatrician). In all cases, a joint visit with the family health visitor with both parents present is optimal.	A well-informed health professional should give information about CF suspected to parents.	Their baby's screening result suggests they may be affected by CF. Their baby will need further tests to confirm this result. Their baby does not need any urgent treatment now; they will receive advice about treatment from the specialist CF team over the next few days.
Give the parents the following resources and information: • 'Cystic fibrosis is suspected' leaflet • time and location of the diagnostic assessment for the following day • 'The sweat test' factsheet (available on the CF Trust website)	Parents will have questions about their baby's results. Parents can quickly forget or misunderstand the information they are given about their baby's results. They may also require access to reliable sources of further information and support.	The time and place of the appointment to see the specialist team and the name of the consultant. They will be able to discuss the screening result and treatment for their baby with the specialist CF team. Where they can get further information and support.
Give the result to the family in the afternoon and offer parents/carers an appointment for the diagnostic assessment with the CF team the following morning.	Delays in confirming results and starting treatment can only add to parents' anxiety.	
Record the result in the personal child health record and in the baby's notes.	Other healthcare professionals have access to the results.	

Appendix 3: Communicating screening results to parents: carrier of CF gene

These guidelines support health professionals to communicate screening results to parents when their baby is a carrier of the cystic fibrosis (CF) gene.

Guidelines for communicating carrier of CF gene screening result	**Reasoning**	**Communication should include the following information**
Inform the family of the probable carrier result promptly. Ideally this is within **24 hours** of the laboratory obtaining the second IRT result.	The family will have raised anxiety levels because a second blood spot sample has been collected. They should have been told the reason for the repeat and when to expect the result. Information on the second blood spot sample is available for healthcare professionals and parents.	
Where possible, the screening laboratory will have a screening nurse specialist who will contact the family health visitor (or preferably a designated health visitor if there is an appointed lead health visitor for giving screening results to families) by phone and confirm in writing.	Health visitors have an ongoing role in supporting families. A well-informed health professional should give information about carrier results to parents.	
The designated health visitor or alternate (who must be trained for the purpose) will visit the family to inform of the result and give them the 'Your baby carries the cystic fibrosis gene' leaflet	Parents will have questions about their baby's results. Giving results over the phone is not satisfactory, as parents may not have any support or source of further information.	Their baby's screening result shows they are a carrier of the CF gene. Carriers are not affected by the condition and do not need any treatment. Where they can get further

	Parents can quickly forget or misunderstand the information they are given about their baby's results. They may also require access to reliable sources of further information and support.	information and support. Carriers can pass on the CF gene to their children, so it is important they tell their child later in life that they are a carrier of the CF gene. It is unlikely that any future children they have will have CF. However, it is possible that both parents are carriers of the CF gene. When both parents are carriers, all future children have a 1 in 4 chance of developing CF. They can find out if they are both carriers by asking their GP for an appointment with a clinical genetics centre.
Tell parents that occasionally there are uncommon alterations of the CF gene that are not recognised by the screening test and therefore there is a small chance that the child will have CF. They should contact their health visitor or GP if they have any concerns about their child's health.	Parents should be aware that there is a small chance that their child could still have CF.	Their baby's screening test shows that they have one copy of the CF gene. However, screening does not identify rarer types of the CF gene. Very occasionally, a child who is thought to be a carrier is diagnosed with CF later in life. If they are worried about their baby's health, they should speak to their GP or health visitor and tell them their baby is a carrier of the CF gene.
Record the result in the personal child health record and in the baby's notes.		