



Public Health  
England



# **NHS Sickle Cell and Thalassaemia Screening Programme Handbook**

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# Chapter 1 - Introduction

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## 1.1 Programme aims:

### **Antenatal screening**

To offer timely antenatal sickle cell and thalassaemia screening to all women (and couples) to facilitate informed decision-making.

### **Newborn screening**

To achieve the lowest possible childhood death rate, and to minimise childhood morbidity from sickle cell disease.

## 1.2 Programme objectives are to:

- ensure a high quality, accessible screening programme throughout England
- support people to make informed choices during pregnancy and ensure timely transition into appropriate follow up and treatment
- improve infant health through prompt identification of affected babies and timely transition into clinical care
- promote greater understanding and awareness of the conditions and the value of screening

This handbook provides supporting guidance for all healthcare professionals throughout the entire screening journey.

The content is based on evidence, healthcare professional enquiries to the programme, lessons from patient safety incidents, data collection, assessment of performance against standards, evaluation of [external SCT courses](#) and the programme's [e-learning resources](#).

## 1.3 Resources

This handbook is part of a suite of documents that include:

- the [service specification](#) which outlines the service and quality indicators expected by NHS England (NHS E) and which meets the policies, recommendations and standards of the NHS Screening Programmes
- the [programme standards \(2017\)](#) explain the standards for monitoring the SCT antenatal and newborn screening programme. The generic [newborn blood spot screening standards](#) also apply
- [the screening pathway](#) a flow chart
- [checks and audits to improve quality and reduce risks](#) explain the checks needed at each stage in the screening pathway to ensure the individual moves seamlessly and safely through the pathway unless they chose not to. If these

checks are not in place there is a risk that an individual does not complete the pathway or the pathway is unnecessarily delayed

- [antenatal and prenatal diagnosis and newborn laboratory handbooks](#) these two handbooks set out policy and standards for laboratories and includes information on:
  - laboratory working standards
  - testing algorithms for antenatal screening
  - referral guidelines for DNA
  - risk assessment procedures
  - laboratory support services

## 1.4 Additional resource

Sickle cell and thalassaemia screening [e-learning](#) module. There are 9 units which can be completed independently. There is an optional quiz to test knowledge at the end of each unit, with a certificate issued on satisfactory completion. The resource covers the following topics:

Unit 1 AN and NB screening for sickle cell, thalassaemia and other haemoglobin variants

Unit 2 understanding haemoglobinopathies

Unit 3 about sickle cell disease

Unit 4 about Thalassaemia

Unit 5 informed choice and understanding diverse needs in screening

Unit 6 understanding the screening test and the FOQ

Unit 7 understanding antenatal screening results

Unit 8 communicating and responding to screening results

Unit 9 screening the newborn infant

## 1.5 Contacting the screening programme

To ensure the handbook meets your needs we require feedback from everyone who uses this resource; please send your comments to [phe.screeninghelpdesk@nhs.net](mailto:phe.screeninghelpdesk@nhs.net)

## Chapter 2 - Support from patient societies

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The UK Thalassaemia Society (UKTS) and the Sickle Cell Society (SCS) are the national charities which represent people affected by thalassaemia and sickle cell disorders respectively. Both Societies collaborate closely with the NHS Sickle Cell and Thalassaemia Screening Programme (NHSSCTSP) in areas such as public outreach, patient engagement, media support, social research, lobbying & campaigning and policy & resource development.

The Societies fully support the NHSSCTSP in its aim to offer informed choice to all couples at risk of having a child affected by a haemoglobin disorder; and the right of parents to exercise this choice. Members of the public can self-refer to both the UKTS and SCS for support and advice about screening. Information about carrier status, and the options available to 'at risk' couples such as prenatal diagnosis or pre-implantation genetic diagnosis (PGD) is also available.

The Societies can provide valuable contacts and information for parents who are at risk of having a child with a haemoglobin disorder; including putting them in touch with other parents and/or affected adults who are successfully managing their condition. It provides evidence that people who have a haemoglobin disorder can, with effective medical management, have similar expectations as other people regarding education, careers and social relationships.

In most cases the Societies can, where necessary, connect people with their peers in terms of language and culture. These contacts can help to inform and reassure parents who have declined PND or who have decided to proceed with an affected pregnancy. The Societies have a unique ability to be able to provide this kind of peer support; which is highly valued by service users. Where relevant, the Societies can also signpost parents to local support groups run by the [NHS Sickle Cell and Thalassaemia Centres \(STANMAP.org\)](#).

All health professionals coming into contact with individuals affected by a haemoglobin disorder (whether carriers, couples at risk or affected individuals); should ensure that they pass on the contact details of the relevant Society and explain that these services are available on request and free to service users.

### **Sickle Cell Society**

54 Station Road,  
London NW10 4UA  
Tel: 020 8961 7795  
Email: [info@sicklecellsociety.org](mailto:info@sicklecellsociety.org)  
Website: [www.sicklecellsociety.org](http://www.sicklecellsociety.org)  
Facebook: Sickle Cell Society UK  
Twitter: @SickleCellUK

### **UK Thalassaemia Society**

19 The Broadway,  
Southgate, London N14 6PH  
Tel 020 8882 0011 or 01226 765 718  
Email: [info@ukts.org](mailto:info@ukts.org)  
Website: [www.ukts.org](http://www.ukts.org)



# Chapter 3 - Understanding Haemoglobinopathies

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All healthcare professionals involved in the screening programme for sickle cell and thalassaemia are advised to keep their knowledge updated; and an [eLearning resource](#)<sup>1</sup> is provided to support practitioners.

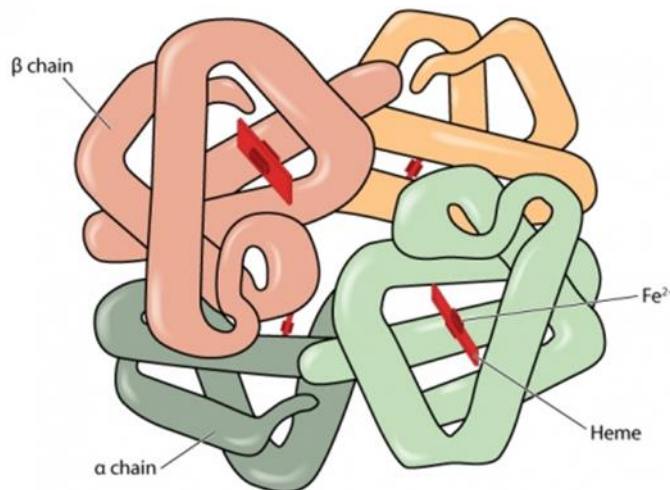
## 3.1 Normal haemoglobin

Haemoglobin (Hb) is the substance within red blood cells which carries oxygen around the body.<sup>2</sup>

Normal haemoglobin is made up of different globin (polypeptide) chains with haem molecules containing iron. The globin chains combine to make particular types of haemoglobin. The structure of each globin chain in haemoglobin is genetically determined.

Normal haemoglobin is called haemoglobin A and consists of:

- 2 alpha ( $\alpha$ ) globin chains
- 2 beta ( $\beta$ ) globin chains



Adult red blood cells normally contain the following haemoglobin chain combinations:

- haemoglobin A ( $\alpha_2\beta_2$ ) >95%
- haemoglobin A<sub>2</sub> ( $\alpha_2\delta_2$ ) 2 to 3.5%
- fetal haemoglobin F ( $\alpha_2\gamma_2$ ) <1%

Laboratory tests can quantify normal haemoglobin and identify variants by their different characteristics.

## 3.2 Haemoglobinopathies: an overview<sup>3; 4</sup>

Haemoglobinopathies are a group of recessively inherited genetic conditions affecting the haemoglobin component of blood. They are caused by a genetic change (mutation) in the haemoglobin. More than 1,000 mutations<sup>5</sup> have been identified that result in either haemoglobin variants or thalassaemias.

Most of these unusual genes are clinically insignificant. However, there is a genetic relevance to some haemoglobinopathies which, when combined with other variants or thalassaemias, may cause a significant clinical condition resulting in illness and potential death.

The most significant haemoglobinopathies result in either a change in the structure and quality of the haemoglobin or a reduction in the quantity of haemoglobin produced.

### **Change in structure and quality of haemoglobin**

Haemoglobinopathies, where the mutation results in a change to the structure and quality of haemoglobin, are known as haemoglobin variants; the most important of which is sickle cell; Hb S. Other haemoglobin variants which have a genetic significance, and occur most frequently in the populations in England are Hb C, Hb D and Hb E\*.

### **Reduction in quantity of haemoglobin**

The thalassaemias is the name for a group of related conditions where the amount of haemoglobin that the body produces is reduced, and this impacts on its oxygen carrying capacity. These usually affect either the alpha or beta globin chain.

**\*Haemoglobin (Hb) E** is technically a Hb variant, but it also interacts with beta thalassaemia to cause a significant clinical condition, so it can be classified in both categories.

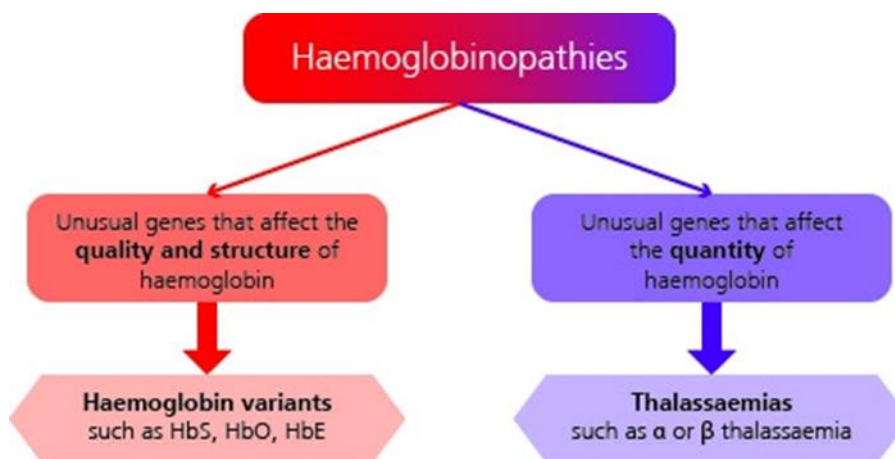
**Haemoglobinopathies** are

- not gender (x) linked
- more prevalent in certain parts of the world. For example sickle cell disease is most common in Africa and India. Thalassaemia major is more common in Asia and Mediterranean countries.

The likelihood of a person being a carrier of a haemoglobinopathy depends on ancestry and the type of mutation varies between ethnic groups.

It is possible to inherit mutations in both alpha and beta globin genes at the same time.

It is also possible (although rare) for an individual to have a 'de novo' haemoglobin mutation. This is a genetic mutation that is not directly inherited from parents, but is present only in that individual.



### 3.3 Inheritance of haemoglobinopathies<sup>6</sup>

The genes for haemoglobin are inherited from both parents. Please refer to the [inheritance risk table](#) for further details.

Haemoglobin disorders such as sickle cell disease or beta thalassaemia major are recessively inherited. If one abnormal beta chain gene is inherited from one parent, the individual will be a carrier of the condition but will not be affected. This is sometimes called having a trait.

Carriers of haemoglobin variants are healthy and unless screened are unaware of their status. A carrier of a haemoglobin variant will usually have approximately:

- 50% normal haemoglobin A
- 30-45% unusual haemoglobin (for example Hb S, Hb C or Hb D)
- a small amount of haemoglobin A<sub>2</sub> and F

Sickle cell carriers have to be careful in certain situations, see the [information for adult haemoglobinopathy carriers - you are a sickle cell carrier](#)<sup>7</sup> leaflet for more information.

Beta thalassaemia carriers may be misdiagnosed as having iron deficiency anaemia but don't require iron therapy. See [information for adult haemoglobinopathy carriers - you are a beta thalassaemia carrier](#)<sup>8</sup> for more information.

An additional range of adult carrier information leaflets can be found at <https://www.gov.uk/government/collections/adult-carriers-sickle-cell-thalassaemia-unusual-haemoglobin><sup>9</sup>

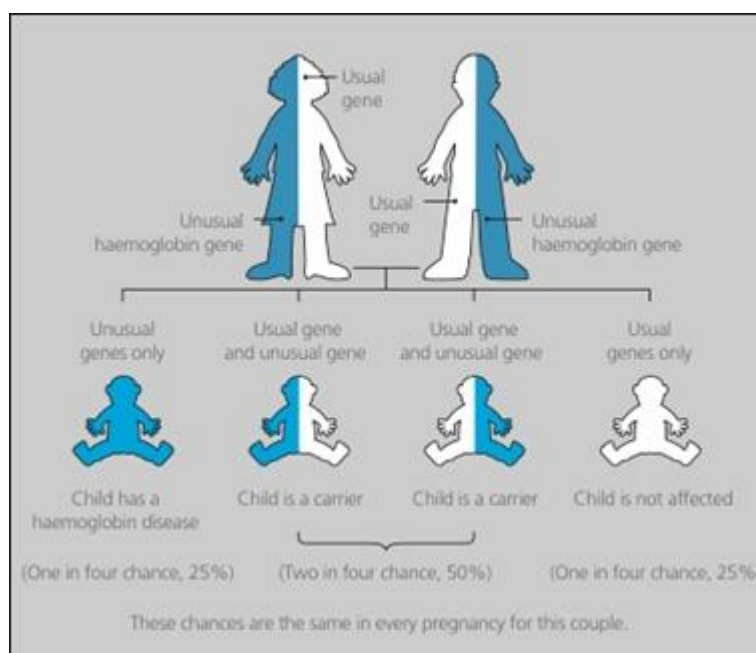
If 2 abnormal beta chain genes are inherited, one from each parent, the individual will have a haemoglobin disorder. The most common clinically significant conditions are thalassaemia major and sickle cell disease.

It is also possible to inherit a **Benign Haemoglobin Disorder**, where the individual has no Hb A, but does not have a clinically significant condition requiring treatment. However, these conditions are genetically relevant.

For more specific information relating to each condition, please refer to haemoglobin carrier states (Appendix 1) and benign haemoglobin disorders tables (Appendix 2).

If both parents carry a haemoglobinopathy in each and every pregnancy the risks to the baby are:

- 1 in 4 (25%) chance of being completely unaffected
- 2 in 4 (50%) chance of being a carrier
- 1 in 4 (25%) chance of inheriting the condition



**It is important parents are aware that the risks are the same for each and every pregnancy.**

### 3.4 Sickle cell disease<sup>10</sup>

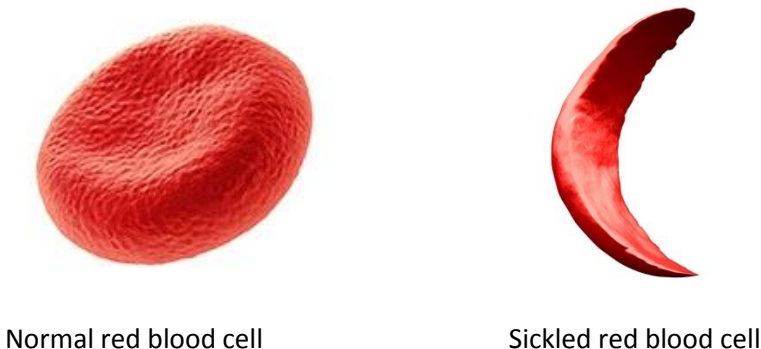
Sickle cell disease is a recessively inherited genetic condition of the haemoglobin. It occurs when both parents pass abnormal haemoglobin genes to the baby, and the baby has no normal haemoglobin (Hb A). The production of abnormal beta globin chains affects the quality of the haemoglobin.

The most common types of sickle cell disease seen in England are:

- Hb SS, sickle cell anaemia
- Hb SC, sickle/Hb C disease
- Hb S/beta thalassaemia

In an individual with sickle cell disease, the red blood cell becomes misshapen and rigid when the haemoglobin becomes de-oxygenated (releases the oxygen to the organs). The red blood cells become sickle shaped and is how the disease got its name. This action is called sickling.

Sickle cell disease most commonly affects people of African, Caribbean, Middle Eastern and Indian ancestry. However, it can affect anyone from any population.



#### **Prevalence of sickle cell disease in England**

Sickle cell disease affects around 1,000 pregnancies per year. Between 260 to 350<sup>11</sup> babies are born with a sickle condition each year. An estimated 12,500 people in England are living with sickle cell disease. It is estimated that there are currently 310,000 sickle cell carriers in England.

#### **Clinical characteristics (Appendix 3)**

Unlike normal red blood cells which move freely in the circulation and have a life span of 120 days, de-oxygenated sickled red blood cells can get stuck and cause blockages in capillaries (small blood vessels), and have a shorter life span of approximately 20 to 30 days. These blockages are known as vaso-occlusive episodes, and are sometimes described as a painful crisis.

A sickle cell crisis can be triggered by:

- sudden changes in body temperature
- dehydration
- shortage of oxygen
- infection

‘Sickling’ can result in:

- intense pain
- severe anaemia
- tissue damage
- infections
- strokes, especially in Hb SS
- shortened life expectancy

These adverse consequences are made worse if the individual experiences repeated crises.

### 3.5 Management of individuals with sickle cell disease<sup>12</sup>

Sickle cell disease requires specialist consultant haematologist or paediatric management. Early diagnosis is vital and screening for sickle cell disease is incorporated in the newborn blood spot screening programme in England. Children who are diagnosed with sickle cell disease at birth should be entered into specialist care by 3 months of age. [See NHS newborn blood spot \(NBS\) screening programme](#) for more information.

Management of individuals with sickle cell disease includes:

- regular specialist outpatient reviews
- easy, direct access to specialist medical care when unwell
- prophylactic penicillin V and regular immunisations to prevent infections
- consideration of hydroxycarbamide if the symptoms are significant
- general anaesthesia should only be undertaken when full medical support is available. This also applies to dental treatment
- blood transfusions may be required for relevant complications, for example stroke or severe/acute anaemia
- annual transcranial doppler scans are recommended for children and adolescents

Sickle cell disease can be cured by bone marrow or stem cell transplant but the genetic profile of the individual does not change.

Much of the care required by individuals with sickle cell disease is preventative and supportive care. Families need specialist support to understand the condition and learn

how to care for children in a proactive way, to recognise potential problems and try to prevent or minimise the effects of a sickle cell crisis.

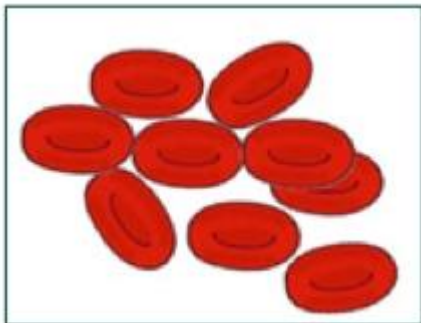
Families are taught to:

- ensure a balanced, healthy diet
- encourage fluid intake
- keep the child warm in cold conditions
- comply with immunisations and penicillin V
- administer simple analgesia at the start of a sickling episode
- seek urgent medical care when required

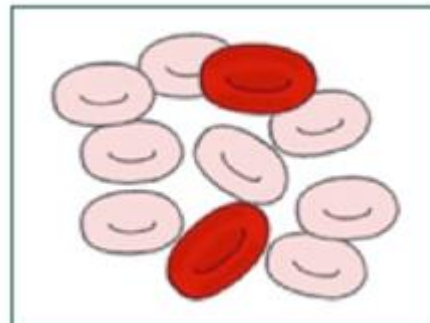
### 3.6 Thalassaemias (Appendix 4)

Thalassaemias are recessively inherited genetic conditions which affect the quantity of haemoglobin produced. This is due to changes in the genetic code responsible for the production of either the alpha **or** beta globin chains that are present in normal haemoglobin. There are 3 types of thalassaemia that have clinical significance. These are:

- alpha thalassaemia major, which is clinically significant to the fetus and mother
- beta thalassaemia major, which is clinically relevant after birth
- thalassaemia intermedia, which has variable clinical significance



Normal red blood cells



Thalassaemic red blood cells



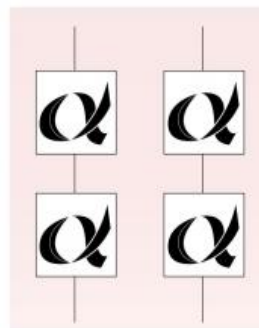
### 3.7 Alpha thalassaemia<sup>13</sup>;

Normal haemoglobin A has 2 alpha globin **chains**, however the production of these alpha globin chains is controlled by 4 alpha globin **genes**, 2 genes from each parent. In alpha thalassaemia there is either reduced or absent production of alpha globin chains, caused by a defect or mutation in one or more of the alpha globin genes.

Alpha thalassaemia carrier status can only be confirmed by DNA analysis.

Below is a graphic illustration of the alpha globin chains (2), and the full complement of alpha globin genes, (4) that each individual with normal Hb A inherits. This is usually written  **$\alpha\alpha/\alpha\alpha$**  in medical literature.

Normal alpha chain profile



### 3.8 Alpha ( $\alpha^0$ ) thalassaemia major

In alpha thalassaemia major, also known as Barts Hydrops Fetalis, there are no functioning alpha globin genes ( $--/--$ ). As a result no alpha globin chains are produced, which results in a severe life-threatening anaemia in the fetus and, without intervention, is incompatible with extra-uterine life.

The hydropic fetus can usually be diagnosed by ultrasound scan during the 2<sup>nd</sup> trimester of pregnancy. Very occasionally, babies survive with intra-uterine transfusions. However, there is a high risk of significant disabilities.

There are also implications for the mother during pregnancy with a fetus that has Barts Hydrops Fetalis, these include:

- pre-eclampsia
- ante-partum haemorrhage
- retained placenta
- possible 50% maternal mortality rate if alpha thalassaemia major in the fetus is undiagnosed



During antenatal screening it is important to diagnose if both parents are alpha zero ( $\alpha^0$ ) thalassaemia carriers, which relies on 3 essential components

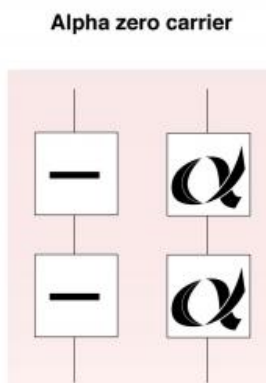
- family origin
- blood tests
- DNA analysis for confirmation of carrier status

The family origins that are most at risk of alpha zero ( $\alpha^0$ ) thalassaemia carrier status are from Taiwan, Laos, Vietnam, Malaysia, China, Hong Kong, Burma, Cyprus, Turkey, Sardinia, Greece, Singapore, Philippines, Thailand, Cambodia and Indonesia.

In the UK around 20 to 30 couples annually are identified as being at high risk of having a baby with alpha thalassaemia major.

### 3.9 Alpha zero ( $\alpha^0$ ) thalassaemia carrier

This occurs when an individual has inherited no alpha globin chain genes from one parent ( $--/\alpha\alpha$ ). The individual is generally healthy but there is a reduction in alpha globin chain production and they may have a mild anaemia with a MCH that is usually less than 25pg. It can be confused with iron deficiency anaemia. Below is a graphic illustration of alpha zero thalassaemia.



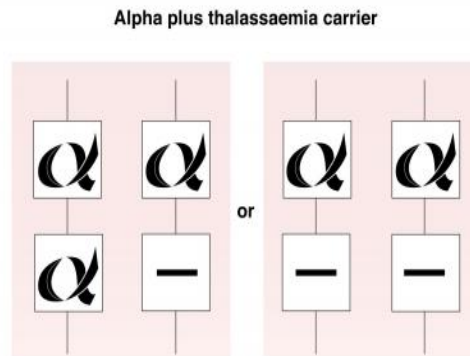
If a couple are both identified as potentially being alpha zero thalassaemia carriers, then their carrier status must be identified by DNA analysis as there is a 1 in 4 (25%) risk to all their children of inheriting Barts Hydrops Fetalis, also known as alpha thalassaemia major.

### 3.10 Alpha plus ( $\alpha^+$ ) thalassaemia

Individuals with alpha plus thalassaemia have inherited either one or 2 faulty alpha globin genes ( $-\alpha/\alpha\alpha$ ) or ( $-\alpha/-\alpha$ ). Although this can affect alpha globin chain production, there is usually minimal change to the haemoglobin level.

Alpha plus thalassaemia is not clinically significant but can be confused with iron deficiency anaemia in the antenatal period.

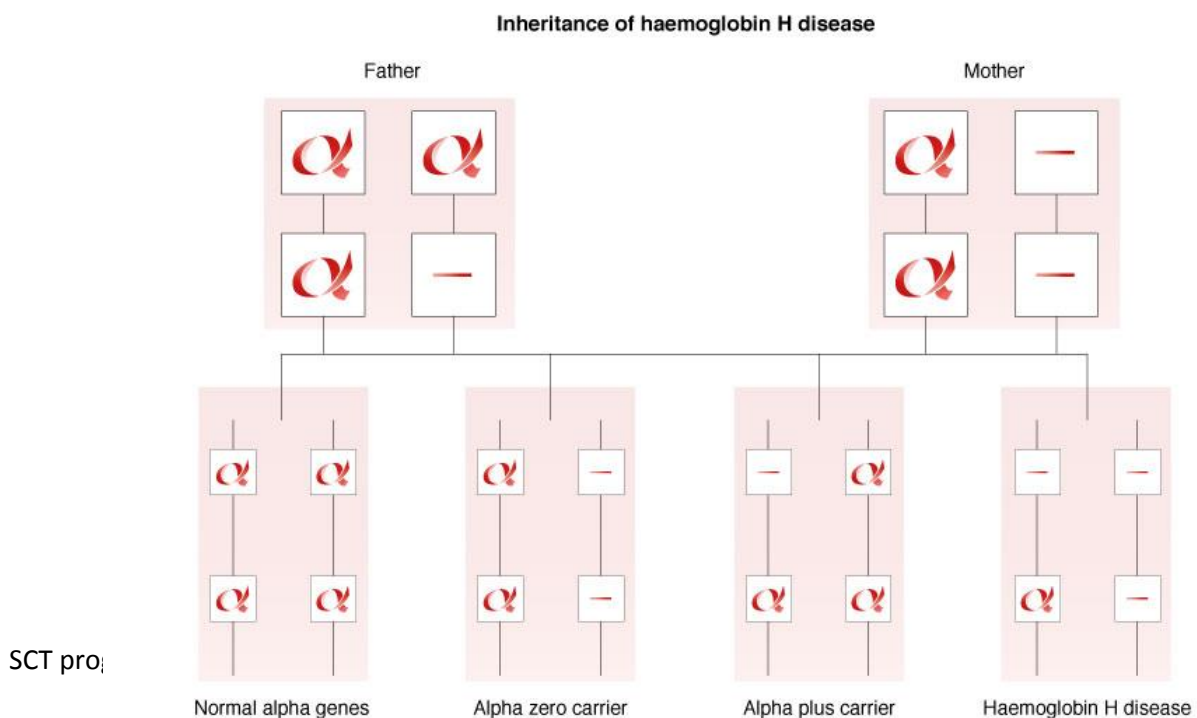
Alpha plus thalassaemia is most often seen in African, Caribbean, Indian, Pakistani, Bangladeshi and Middle Eastern populations.



### 3.11 Haemoglobin H disease

An individual with haemoglobin H disease ( $--/-\alpha$ ) has only one normal alpha globin gene but usually retains the ability to produce sufficient haemoglobin for life. The haemoglobin level usually ranges from 7 to 10g/dl, with a MCH of 15 to 25pg.

Haemoglobin H disease is a mild to moderate condition. It does not usually require treatment or lifelong blood transfusions, however short-term transfusions may occasionally be required during critical periods, such as pregnancy or illness or if the individual has an infection.



### 3.12 Beta Thalassaemia major <sup>14</sup>

Beta thalassaemia major is also called 'Cooley's Anaemia' or 'Mediterranean Anaemia'.

Thalassaemia major is most common in people of Pakistani, Cypriot, Italian, Greek, Indian, Bangladeshi, Chinese and other East/South East Asian ancestry.

There are 2 main thalassaemia conditions depending on the beta thalassaemia gene mutation inherited. They are:

- thalassaemia major
- thalassaemia intermedia

In beta thalassaemia major there is reduced or absent production of the beta globin chains that make up normal adult haemoglobin, due to defective beta globin genes which are inherited from both parents. This results in severe, life-threatening anaemia which usually requires regular blood transfusions for life.

#### **Prevalence in England**

It is estimated that thalassaemia major affects about 1 in 27 000 pregnancies. Approximately 20-30<sup>5</sup> babies are born with thalassaemia major each year. There are more than 800 people living with thalassaemia major.

It is estimated there are 300 000 thalassaemia carriers.

#### **Clinical complications of untreated beta thalassaemia major**

Clinical complications of untreated beta thalassaemia major include:

- failure to thrive in babies and young children
- lethargy and fatigue due to severe anaemia
- hypersplenism due to impaired breakdown of red blood cells
- over activity of the bone marrow
- severe anaemia leading to early death

### 3.13 Management of individuals with beta thalassaemia major

Although beta thalassaemia major is not included in the newborn bloodspot screening programme, children with this condition are usually identified and should be referred for specialist care. Early diagnosis helps to monitor a child's condition until blood transfusions are required and also gives parents the opportunity to learn about the condition before complications arise. .

The management of individuals with beta thalassaemia major aims to correct the severe anaemia and includes

- blood transfusions every 3 to 5 weeks, usually starting from approximately 9 to 12 months of age
- iron chelation therapy to remove the excess iron (either orally or by subcutaneous injection)
- regular hospital appointments to monitor the condition
- splenectomy for hypersplenism

In addition, supportive care is important for people affected by beta thalassaemia major and they

- should be encouraged to avoid iron rich foods and have a daily vitamin C supplement
- may require bone marrow or stem cell transplant to cure their condition, however their genetic profile does not change
- should have psycho-social support in addition to medical care

There is a risk of early death unless patients adhere to the strict regime of blood transfusions and iron chelation.

#### **Clinical complications of treated beta thalassaemia major**

If thalassaemia major is not well managed by transfusion therapy this could result in anaemia and over-activity of bone marrow. However, the major cause of complications is usually related to an excess of iron accumulated in the body due to the regular blood transfusions. This can result in the following

- damage to the pituitary glands which could affect
  - growth and also delayed puberty
  - insulin production, resulting in diabetes
- hypothyroidism
- cardiac impairment/failure
- liver damage
- lethargy and fatigue
- erectile dysfunction in men and amenorrhoea in women
- change in skin colour due to iron deposits

Individuals may also have

- hypersplenism due to impaired breakdown of red blood cells and over activity
- increased susceptibility to infections such as meningitis and flu, especially if the spleen has been removed

### 3.14 Thalassaemia intermedia

Thalassaemia intermedia occurs in an individual when the beta globin chain production is significantly reduced. Clinical implications vary depending on the gene mutations inherited from both parents. This can result in a degree of anaemia, but the condition is not as severe as thalassaemia major.

The individual usually manages without regular blood transfusions but there may be splenomegaly and the requirement for occasional blood transfusions.

### 3.15 Haemoglobin E/beta thalassaemia

Haemoglobin E/beta thalassaemia may result in a syndrome similar to either thalassaemia major or thalassaemia intermedia.

### 3.16 References

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<sup>2</sup> Sickle Cell Information Centre (SCINFO) *Tutorial: Normal Blood Cells* <http://scinfo.org/world-wide-resources/power-point-presentations>

<sup>3</sup> Bain BJ (2006) *Other significant haemoglobinopathies*. Haemoglobinopathy Diagnosis, 2<sup>nd</sup> Edition Blackwall Publishing Ltd

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<sup>7</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2012) *Information for adult haemoglobinopathy carriers: you are a sickle cell carrier* <https://www.gov.uk/government/publications/sickle-cell-carrier-description-in-brief>

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<sup>8</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2012) *Information for adult haemoglobinopathy carriers: you are a beta thalassaemia carrier.* <https://www.gov.uk/government/publications/beta-thalassaemia-carrier-description-in-brief>

<sup>9</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2012) *Adult carriers: sickle cell, thalassaemia, unusual haemoglobin* <https://www.gov.uk/government/collections/adult-carriers-sickle-cell-thalassaemia-unusual-haemoglobin>

<sup>10</sup> Eleftheriou A, Angastiniotis M *About Sickle Cell Disorders.* Thalassaemia International Federation (TIF) <http://www.thalassaemia.org.cy/>

<sup>11</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2017) *Sickle cell and thalassaemia screening: data trends and performance analysis* <https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-data-trends-and-performance-analysis>

<sup>12</sup> Brent Sickle Cell & Thalassaemia Centre (2012) *A Parent's Guide to Managing Sickle Cell Disease* <https://www.gov.uk/government/publications/sickle-cell-disease-managing-the-condition>

<sup>13</sup> Eleftheriou A, Angastiniotis M *About Alpha Thalassaemia* Thalassaemia International Federation (TIF) [www.thalassaemia.org.cy](http://www.thalassaemia.org.cy)

<sup>14</sup> Eleftheriou A, Angastiniotis M *About Beta Thalassaemia* Thalassaemia International Federation (TIF) [www.thalassaemia.org.cy](http://www.thalassaemia.org.cy)

# Chapter 4 - Antenatal Screening

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Antenatal screening identifies women with a haemoglobinopathy, and provides screening of consenting biological fathers. When both parents are carriers of a significant haemoglobinopathy, there is a one in four (25%) chance, in each pregnancy, that their baby could inherit a condition that needs treatment. The most important conditions are sickle cell disease and thalassaemia major.

[Sickle cell disease and thalassaemia major](#) are serious, inherited blood disorders. They affect haemoglobin and its oxygen carrying capacity. Individuals who have one of these conditions need treatment and lifelong care. People who are carriers are healthy and unaware of their status unless they have a specific blood test.<sup>15</sup>

Carrier women and couples “at risk” of having a baby with a major haemoglobin disorder need information, advice and counselling to make choices for the pregnancy. This includes the decision to have prenatal diagnosis, and to take further action if they choose to.

This means that screening must occur early in pregnancy, preferably by 10 weeks’ gestation. This allows time for any subsequent actions required. Early screening usually results in a greater uptake of prenatal diagnosis (PND), ideally by [12 weeks + 6 days gestation](#).<sup>16</sup>

The antenatal screening programme is a [pathway](#)<sup>17</sup> and needs all the components in place for the screening test to be effective. The stages in the pathway work most efficiently with coordination from a multidisciplinary team of professionals. These include:

- midwife, screening coordinator, & maternity services
- laboratory team
- counselling services
- primary care
- voluntary sector

To ensure that a quality service is delivered, there must be a named individual who has lead responsibility for each stage of the pathway:

- identification of the eligible population
- providing information before screening and completion of the [Family Origin Questionnaire \(FOQ\)](#),<sup>18</sup> along with obtaining a blood sample
- processing the blood samples and reporting the results
- offer of testing to all biological fathers of babies where the mother has been identified with a haemoglobinopathy
- communicating the blood test results to mother and the baby’s father (where relevant)
- carrying out actions, such as prenatal diagnosis, based on parental decisions
- diagnosis (where requested) of babies at risk of inheriting a major haemoglobin disorder
- refer affected individuals for treatment and care

## 4.1 Prevalence

There are two approaches to the delivery of the screening programme based on the geographical [prevalence](#) of haemoglobinopathy conditions in the high risk populations living in England.<sup>19</sup> A [list of high and low prevalence trusts](#) is available for further information.

**In low prevalence trusts**, where less than 1% of the booking bloods received by the laboratory are screen positive:

- with consent, the red blood cell indices will screen all women (irrespective of family origins) for thalassaemia
- the [FOQ](#) is used as an initial screening tool to identify women, or the baby's biological father, at high risk of being a carrier for sickle cell, and other haemoglobin variants
- where either parent falls into a high risk group, a screening blood test for haemoglobin variants must be offered to the woman

**In high prevalence trusts**, where 2% or greater of the booking bloods received by the laboratory are screen positive

- all women must be offered a screening blood test for sickle cell, thalassaemia and other haemoglobin variants, irrespective of family origins

**In high and low prevalence trusts**

- where a woman is diagnosed with a haemoglobinopathy, the baby's biological father (irrespective of family origins) must be offered screening for sickle cell, thalassaemia and other haemoglobin variants
- it is important to note that not all haemoglobinopathies will be diagnosed and where there is an inconclusive result, systems must be in place to follow up the woman/couple where relevant
- a completed paper or electronic FOQ must accompany all blood samples to the laboratory
- [checks](#) should be in place to ensure that all women have been offered screening, and the results have been followed up appropriately

There are detailed algorithms for processing antenatal samples in both high and low prevalence areas, which are outlined in the [Laboratory Handbook](#).<sup>20</sup>



## 4.2 Booking for antenatal care

### Choice & Consent<sup>21</sup>

All women must receive information about antenatal screening tests early in pregnancy, before they are asked to make any screening decision. This should include information on when results will be available following uptake of screening.

There must be an opportunity to discuss the screening options with a professional who is informed about the condition(s). The health professional offering the screening test must ensure that the woman understands the test, has given her consent for antenatal screening, and is aware of the choices that will follow if the test is positive.

When **offering screening** for sickle cell and thalassaemia, healthcare professionals (HCPs) must:

- give verbal and written information about the screening test, using the booklet [Screening tests for you and your baby](#)<sup>22</sup>
- offer the woman an opportunity to discuss the screening test and her decision
- offer resources to address any specific needs that the woman has such as literacy, visual impairment, language needs<sup>23; 24</sup>
- be aware of, and sensitive to, the woman's values and beliefs and support the woman to make decisions which are right for her
- record consent or non-consent for screening in the woman's maternity notes
- communicate non-consent for screening to appropriate professionals, including laboratory staff

It is only necessary to offer screening for sickle cell and thalassaemia once in the same pregnancy. If a woman is screened in a low prevalence area, but chooses to give birth in a maternity unit in a high prevalence area, her current result is sufficient, and there is no need for re-screening.

Alternately, if the woman changes NHS provider during the pregnancy, it is not necessary to repeat the blood test if the result is available.

In both cases the previous result must be from a laboratory accredited by [the UK Accreditation Service \(UKAS\)](#), and be consistent, unequivocal, well documented and interpreted and reported within the testing algorithms in the [laboratory handbook](#).<sup>20</sup>

During **booking for antenatal** care it is important to establish some details which are relevant to the sickle cell and thalassaemia screening programme. This includes information about:

- adoption or a lack of awareness of family ancestry from either parent?
- fertility treatment, is it a
  - donor egg?
  - donor sperm?
  - both?
- history of blood transfusion or currently having regular blood transfusions? (Why? When? Where?)
- history of bone marrow or stem cell transplant? (Why? When? Where?)

- history of haemoglobin disorders or other inherited conditions? For themselves? In either the maternal or paternal family?

If the woman consents, the screening sample must be taken at first booking appointment.

If the woman **declines** screening, the laboratory team should be aware of this information prior to processing the full blood count sample. All women need to be made aware that routine analysis of blood may be indicative of thalassaemia carrier status. However, further investigations to confirm carrier status should not occur if the woman has not consented to screening.

### 4.3 The family origin questionnaire (FOQ)

Although people from any population can have these conditions, it is more likely that an individual will be a genetic carrier if any of their ancestors come from a malarial area of the world. Being a carrier provides partial protection against malaria.

The aim of the [FOQ](#)<sup>25</sup> is to identify the population groups at highest risk of sickle cell, thalassaemia and other haemoglobin variants.

Completion of the FOQ information is the responsibility of the HCP who is booking the woman for antenatal care. Details are required:

- for both the baby's biological mother and father
- in both high and low prevalence areas
- to be completed in every pregnancy and sent with the blood sample to the laboratory, or be accessible to the laboratory team if using an electronic system
- for **all** ancestry, as far back as the individual can remember (at least 2 generations, but more if possible); this is particularly important for mixed race individuals

In **low prevalence** areas the FOQ information is used as an initial screening tool which asks about the family origins of both parents, to assess a woman's eligibility for haemoglobin variant screening. If the woman falls into a high risk group she should be offered screening for haemoglobin variants

If the woman falls into a low risk group, but the baby's biological father falls into a high risk group, then the woman should be offered screening for a haemoglobin variant (irrespective of her family origins).

In **high and low prevalence** areas the FOQ

- must accompany all blood samples to the laboratory, or the relevant information must be accessible to the laboratory team if using electronic requesting
- can avoid unnecessary testing of fathers and unnecessary anxiety for parents when accurately completed

- is relevant in the interpretation of red blood cell indices, particularly when screening groups at high risk of alpha zero thalassaemia
- assists with accurate DNA analysis of prenatal diagnosis samples, ensuring that the relevant genotypes are included in the assay

If the woman **declines** screening, there must be systems in place to inform the laboratory team of this information.

The NHS Sickle Cell and Thalassaemia screening programme produces a paper FOQ form as a template. The integration of the FOQ categories onto local antenatal screening forms or incorporated into an electronic requesting system is encouraged. The versatility of the national template must be reflected locally and the categories kept up to date if there are any changes.

The current [FOQ](#) form can be downloaded from the programme website and can also be ordered from [Harlow Press](#).

#### 4.4 Conditions & carrier states to be detected<sup>26</sup>

There are over a thousand haemoglobin variants and thalassaemia mutations, but not all of these are clinically relevant.<sup>27</sup> The national programme in England has determined the significant haemoglobinopathies which must be detected by antenatal screening.<sup>20</sup> The rationale for choosing these carrier states and conditions is based on the high risk populations living in England.

##### 1. Significant maternal haemoglobin conditions (these are important for maternal care)

- Hb SS
- Hb SC
- Hb SD<sup>Punjab</sup>
- Hb SE
- Hb SO<sup>Arab</sup>
- Hb S/Lepore
- Hb S/ $\beta^{(0; +)}$  thalassaemia
- Hb S/ $\delta\beta$  thalassaemia
- $\beta$  thalassaemia major/intermedia
- Hb Lepore/ $\beta$  thalassaemia
- Hb E/ $\beta$  thalassaemia
- Hb H Disease ( $--/\alpha$ )

##### 2. Carrier states in mother

- Hb AS
- Hb AC
- Hb AD<sup>Punjab</sup>
- Hb AE
- Hb AO<sup>Arab</sup>
- Hb A/Lepore

- $\beta$  thalassaemia carrier
- $\delta\beta$  thalassaemia carrier
- $\alpha^0$  thalassaemia carrier ( $--/\alpha\alpha$ )
- Hereditary persistence of fetal haemoglobin (HPFH) carrier

**3. Any compound heterozygous state including one or more of the above carrier states.**

**4. Any homozygous state of the above carrier conditions.**

#### 4.5 Screening for haemoglobin variants

In low prevalence areas the information about both the woman and the baby's biological father on the family origin questionnaire, along with her consent, determines which women must be screened for haemoglobin variants.

In high prevalence areas all consenting women are screened for haemoglobin variants, irrespective of their family origins.

#### 4.6 Screening for beta thalassaemia

All women in both high and low prevalence areas should be offered screening for thalassaemia.

The initial screen for the risk of thalassaemia involves a review of the full blood count:

- haemoglobin (Hb) – normal value in pregnancy is equal to, or above  $\geq 11$  g/dl. Low values may indicate anaemia
- mean cell volume (MCV) - normal range is 77-95 fl. Low values may indicate deficient haemoglobin production such as iron deficiency anaemia or thalassaemia
- mean cell haemoglobin (MCH) – normal range is 27-32 pg. Low values are seen in thalassaemia or iron deficiency anaemia

If the MCH is lower than usual, the Hb A<sub>2</sub> is measured. A range between 3.5% - 8% is the usual for a beta thalassaemia carrier. Screening for beta thalassaemia can sometimes be complex.<sup>27</sup>

#### 4.7 Screening for alpha zero thalassaemia

There is no straightforward test in the antenatal screening laboratory to diagnose an alpha thalassaemia carrier, and DNA is required for a definitive diagnosis. The approved laboratories for DNA testing are listed in the Laboratory Handbook<sup>20</sup> and Appendix 5.

**Alpha<sup>+</sup>** (alpha plus) thalassaemia is not considered clinically significant, and a suspected carrier will not require any further investigations.

**Alpha<sup>0</sup>** (alpha zero) thalassaemia is clinically significant and most commonly found in people with ancestry from

- East Mediterranean (Cyprus, Greece, Sardinia or Turkey)
- Southeast Asia (China, Hong Kong, Thailand, Taiwan, Cambodia, Laos, Vietnam, Burma, Singapore, Indonesia or Philippines).

The screening policy in England aims to identify couples where both parents are alpha zero thalassaemia carriers (alpha<sup>0</sup>) and their baby is at risk of inheriting alpha thalassaemia major (Hb Barts Hydrops Fetalis). The screening process to follow for these couples:

- if the woman's initial screening result indicates that she may be an alpha zero thalassaemia carrier, but only one parent is from a high risk group and the other parent is not, then no further investigations are needed
- if the woman's initial screening result indicates that she may be an alpha zero thalassaemia carrier, and both biological parents are from one of the high risk groups (see list above), then the baby's father should be offered a screening test
- if both parental screening results show a possibility of alpha zero thalassaemia carrier status, then a blood sample from each parent must be sent for DNA analysis to confirm whether or not they are alpha zero thalassaemia carriers
- if both parents are carriers, then prenatal diagnosis (PND) should be offered

Only a small number of cases of alpha thalassaemia major occur in England each year.<sup>28</sup>

#### 4.8 Referral of antenatal samples to the DNA laboratories for haemoglobinopathy mutation analysis<sup>20</sup>

The majority of carriers are diagnosed in the antenatal screening laboratory. However, on occasion it may be necessary to refer a sample for DNA analysis. It is the responsibility of the antenatal screening laboratory team to decide which samples need to be referred and to inform the maternity or counselling team if any additional blood samples are needed from either the woman or the baby's biological father.

## 4.9 Issues which may arise during routine antenatal screening

During screening some carriers may be missed, and it is possible for false positive and false negative results to be reported. Assuming that the FOQ has been completed accurately, below are some examples of carrier states that can be missed<sup>20</sup>

- Some  $\beta$ -thalassaemia carriers may have
  - a “silent” or “near silent” genotype, associated with a borderline Hb A<sub>2</sub> level
  - their carrier status obscured by severe iron deficiency anaemia; a medical condition (B12 or folate deficiency; liver disease); or treatment (such as HIV therapy); or another haemoglobinopathy
- alpha<sup>0</sup> thalassaemia occurring outside the defined high risk family origins or in women with anaemia
- any significant haemoglobin masked by an unreported blood transfusion or bone marrow transplant
- any significant haemoglobinopathy present in donor egg or donor sperm where the donor is undeclared or untested
- a second haemoglobin variant may be masked by haemoglobin A or another haemoglobinopathy.

In **low prevalence** areas, in addition to the above, carrier states that occur in individuals who fall outside the defined high risk family origins, or in individuals who have not disclosed their family origins accurately, may be missed.

## 4.10 Testing in subsequent pregnancies

If a woman is booked for antenatal care for a subsequent pregnancy, the HCP must:

- offer the woman screening for a haemoglobinopathy, irrespective of previous screening
- complete the **FOQ**, or have systems in place to make the information accessible to the laboratory team if using electronic test requesting
- take the blood sample and send to the laboratory, if the woman consents to screening

If a carrier or affected woman is identified, the baby’s biological father must be offered a screening test, irrespective of previous screening history. If it is not possible to test the baby’s biological father in every pregnancy and a previous result is being considered for use, please check that this is the same father. This information must be recorded in the woman’s notes for the current pregnancy. If a written copy of the result is available, this should also be included in the woman’s records.

The previous result must be from a laboratory accredited by the [UK Accreditation Service \(UKAS\)](#), and be consistent, unequivocal, well documented and interpreted and reported within the testing algorithms in the [Laboratory Handbook](#).<sup>20</sup>

## 4.11 Screening results<sup>28, 29</sup>

Screening results should be reported within 3 working days following receipt of the blood sample in the laboratory. On occasion, if further investigations are required, an interim report will be provided until the final report is available. The expectation is that the midwife will act on this interim report and initiate screening of the baby's biological father, if he is available.

If nothing abnormal is detected on the father's result, then the risk to the baby of inheriting a major haemoglobin disorder can be excluded.

If the baby's biological father is unavailable for screening, a confirmed maternal result is required before prenatal (PND) can be offered, and should not be performed based on interim results alone.

The laboratory will report one of the following:

- **No abnormality** detected, Hb AA; approximately 97% of women screened will have this result. No testing of the biological father is required.
- **Non-significant carrier.** Not clinically significant and there is no risk to the baby of inheriting a major haemoglobin disorder. No testing of the biological father is required.
- **Significant carrier.** This is clinically significant and the baby may be at risk of inheriting a major haemoglobin disorder if both parents are carriers. Around 2.5% or 1 in 40 pregnant women will be identified as carriers. Testing of the biological father is required.
- **Benign haemoglobin disorder** (for example: Hb CC, Hb DD, Hb EE). The woman must be referred for a haematology consultation but often no special care during pregnancy is necessary. Screening of the biological father is required and the baby may be at higher risk (50% chance) of inheriting a haemoglobin disorder if the father is a carrier of a significant haemoglobinopathy.
- **Clinically significant disorder** (sickle cell disease [eg Hb SC] or thalassaemia condition). Most of these women are aware of their condition but on occasion this may be identified for the first time during antenatal screening. Urgent referral to haematology and consultant obstetric teams is needed. Joint medical and obstetric care and close monitoring throughout the pregnancy is necessary, and women should be booked for a hospital delivery.

Testing of the baby's biological father is required. There is a higher risk (50% chance) of the baby inheriting a haemoglobin disorder if the biological father is a carrier of a significant haemoglobinopathy.

- **Inconclusive result** - further testing of the woman may be required depending on the variant suspected. The process to be followed for these couples:
  - o the result should be explained to the woman
  - o testing of the baby's biological father should be offered
    - if he **does not** have a haemoglobinopathy there is no risk of the



baby inheriting a major haemoglobin disorder. There may be no further maternal testing required (this is locally determined).

However, if there is no further testing of the woman she will remain unaware of her specific carrier status, and the risks for offspring in a future pregnancy if she changes partners

- if he **does have** a haemoglobinopathy, then further maternal testing may be required for an accurate assessment of the fetal risk of inheriting a significant haemoglobin condition, and the couple need to be followed up appropriately

All women should be informed of their screening result (normal, carrier, inconclusive, haemoglobin disorder) and a local protocol and pathway must be in place to support this.

Women who have inconclusive, carrier or affected results should be offered an opportunity to receive the result in a face to face counselling session, along with written notification of the results.

An [information leaflet](#) on specific carrier status must be provided.<sup>30</sup> Advice regarding issuing haemoglobinopathy cards is given by the [British Society of Haematology \(BSH\)](#)<sup>26</sup>

Screening results should be accessible to ALL HCPs involved in the screening programme by recording details in the woman's:

- handheld maternity records
- electronic maternity record
- primary care health record

#### 4.12 Screening follow up for clinically significant results (carrier, affected, inconclusive, benign haemoglobin disorder)

Results must be communicated to the woman urgently. The mother needs time to organise screening for the baby's biological father and to consider the implications for the pregnancy and her unborn child. Receiving a positive screening result can be emotionally traumatic for women, as this may not have been anticipated. A [trained](#) professional should be available to explain all significant results.

Timing is critical in making decisions for further investigations. Women should be given written confirmation of their result along with an explanatory [leaflet](#).<sup>30</sup> The woman must be invited for counselling<sup>31</sup> (a [template letter](#) is available) and made aware of:

- the implications for her as an individual of being a carrier or having a haemoglobin condition
- the implications for this pregnancy and for future pregnancies
- the fact that the baby's biological father needs to be tested to assess the risk to the baby
- the available choices for the pregnancy
- the fact that other members of her family could also be carriers and that they can request testing by their GP or at a specialist centre, especially if they are planning to have a baby



### 4.13 Beta thalassaemia carriers

A beta thalassaemia carrier has inherited an abnormal beta globin gene from one parent and a normal one from the other. Where an individual is a beta thalassaemia carrier it is important for them to be aware of the fact that:

- the abnormal gene could be passed on to his or her children
- even if their child has inherited the gene it cannot be diagnosed at birth by routine newborn blood spot screening
- if parents choose, babies can be tested when they are over 9 months of age to confirm their carrier status

An example of a counselling form that could be used is in Appendix 6.

### 4.14 Screening the baby's biological father

During organising and encouraging screening of the baby's father, HCPs should be sensitive to possible paternity issues, and clarify to the woman the importance of screening the baby's biological father.

The baby's biological father of **all** women identified with a haemoglobinopathy, or an inconclusive result, (irrespective of his family origins), should be invited for counselling and a blood test as soon as possible. The leaflet, [Tests for Fathers](#)<sup>32</sup> and [letter](#)<sup>33</sup> should be given to the father prior to screening. Fathers must be offered screening in every pregnancy as for mothers.

Where possible the couple should have a joint counselling session to discuss the woman's results and the implications for the pregnancy, and for the father to be tested. The session should be with a professional [trained](#) in giving haemoglobinopathy information.

If a joint appointment is not possible, then the father should be offered an appointment on his own to discuss the screening results and to have a blood test.

The HCP responsible for screening the baby's biological father should provide the laboratory with information about the woman when the father is screened so that the results can be linked.

The [fathers](#)<sup>34</sup> test result should be recorded in the mother's antenatal handheld records and on the counselling records.

### 4.15 Maximising uptake of father testing

On occasion it may be difficult for biological fathers to attend for screening, or they may be reluctant to be screened.

Some of the possible barriers to accessing screening include:

- an assumption by the man that he has already been tested and has a negative result (based on the fact that he may have had a blood test in the past)

- a lack of understanding about the test; the significance of being a carrier; how the conditions are inherited; the risk to their baby
- a possible stigma attached to screening
- men who think that if they are well they cannot be a carrier
- pregnancy and blood tests are seen as being a part of the woman's world, compounded by systems in the antenatal clinic
- difficulty with taking time off work to attend an appointment for a blood test
- fear of needles

Some men may have been previously screened, either in the UK or in another country, and do not recognise the need for re-screening. Explain that

- it is necessary for their previous result to be confirmed when having prenatal diagnosis (PND)
- previous screening may not include all variants tested for in the English Programme
- screening test results need to be from an accredited laboratory
- we need to see a copy of the laboratory report with his previous screening result

**The HCP who reviewed the father's previous screening results should document this in the woman's record and, where possible, keep a copy of the result.**

#### **Some points to consider**

- timing - can screening be offered at a convenient time for the father e.g. outside his normal working hours?
- location - can screening be offered at a more convenient or neutral location?
- if there are socio-cultural barriers to uptake, listen to what the mother says
- would direct contact from the HCP to the father support the request for the need to have a blood test, and highlight the importance of screening?

#### **Biological father unavailable for screening**

If the baby's biological father is **unavailable**, unknown or refuses testing then the HCP should discuss options with the woman:

- is she living with the father/in contact during this pregnancy?
- has the biological father been tested in the past and is there a confirmed result?
- is she willing (or able) to deliver the letter and leaflet to the father?
- if she is not living with the father and no longer in contact, can she provide his details so that the information about the test can be sent to him directly?

The responsible HCP should attempt to make direct contact with the baby's biological father, with the woman's consent, if the woman is unwilling or unable to make contact, in order to offer information and a screening blood test.

## 4.16 Follow up after paternal screening<sup>29</sup>

Results should be reported to the designated HCP within 3 working days from the time of blood sample receipt in the laboratory.<sup>16</sup> All father screening results must be reviewed and linked to the maternal results. [Checks](#) should be in place to ensure that [paternal results](#)<sup>34</sup> have been received and are followed up.

Fathers must be informed of their results, whether or not these are clinically significant. Carriers should receive the information in writing, along with an appropriate [carrier leaflet](#)<sup>30</sup> where relevant.

Advice regarding issuing haemoglobinopathy cards is given by the [British Society of Haematology](#) (BSH).<sup>26</sup>

### 4.16.1 Paternal carrier results (baby at risk of inheriting a benign haemoglobin disorder)

If the man is identified as a haemoglobinopathy carrier then the couple must be invited for a follow up counselling session and the results explained “face to face”.

If the couple are at risk of having a baby with a benign haemoglobin disorder which does not require long-term treatment, (for example a condition such as Hb EE; Hb CC; Hb DD; Hb C/Beta thalassaemia), this should be explained and the couple reassured. Confirmation in writing of his carrier status and an appropriate [carrier leaflet](#)<sup>30</sup> should be given to the father.

Prenatal diagnosis is **not** required for any of these conditions.

### 4.16.2 Paternal carrier results (baby at risk of inheriting a major haemoglobin disorder)<sup>35</sup>

Women and couples “*at risk*” of having an affected baby must be offered prenatal diagnosis (PND) as soon as possible, ideally by 12 weeks + 0 days gestation. They should

- be offered an urgent counselling appointment with an appropriately trained professional (for example a professional trained in an approved course such as the [genetic risk assessment and counselling course](#)) to explain the risk to their baby, details about the condition that their baby could inherit, and the options for the pregnancy. An explanatory leaflet<sup>36; 37</sup> to support the counselling session should be given to the couple
- be urgently referred if they do decide to proceed with prenatal diagnosis

## 4.17 Considerations for the antenatal screening programme

The Sickle Cell and Thalassaemia Screening Programme presents some challenges for practitioners.

- **Defining family origins, heritage and ancestry:**

Identifying family origins, heritage or ancestry is integral to screening for sickle cell and thalassaemia. It is important this is not confused with nationality.

The FOQ identifies the groups at highest risk of sickle cell, thalassaemia and other haemoglobin variants. This includes the Mediterranean population who, under normal circumstances, may be 'missed' for screening. Practitioners need to assist parents to complete the FOQ for screening in low prevalence areas and for laboratories to have the correct information for analysis of samples.

- **Influences of culture during screening:**

The perception of what carrier status means may affect families' attitudes to screening. In some of the groups at highest risk of haemoglobinopathies, there may be religious or cultural beliefs that influence decisions about prenatal diagnosis and termination of pregnancy. Research<sup>38</sup> confirms this and practitioners need to be aware of the relevant issues.

- **Linking the antenatal and newborn screening programmes:**

The national programme in its entirety is a linked antenatal and newborn screening programme. The genetic nature of sickle cell disease and thalassaemia major means that it is important to link information from parental results to the baby's screening result. Local systems need to be in place to facilitate this.

## 4.18 References

- 
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- <sup>23</sup> NHS Sickle Cell & Thalassaemia Screening Programme *Large Print information* <http://webarchive.nationalarchives.gov.uk/20150408175925/http://sct.screening.nhs.uk/easyreadlargeprint>
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- <sup>27</sup> Huisman THJ et al *A database of Human Hemoglobin Variants and Thalassemias* <http://globin.bx.psu.edu/cgi-bin/hbvar/counter>
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- <sup>34</sup> Fatherhood institute (2012) *Guidance Contacting fathers for antenatal sickle cell and thalassaemia screening* <https://www.gov.uk/government/publications/contacting-men-for-sickle-cell-and-thalassaemia-screening/contacting-fathers-for-antenatal-sickle-cell-and-thalassaemia-screening>
- <sup>35</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2017) *Counselling and Referral for Prenatal Diagnosis – Chapter 5 Programme Handbook*
- <sup>36</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2015) *Information for couples “at risk” of having a baby with sickle cell disease or thalassaemia major* <https://www.gov.uk/government/publications/baby-at-risk-of-having-sickle-cell-disease-description-in-brief> and <https://www.gov.uk/government/publications/baby-at-risk-of-having-thalassaemia-description-in-brief>
- <sup>37</sup> Fetal Anomaly Screening Programme (2017) *Diagnostic tests* <https://www.gov.uk/government/publications/cvs-and-amniocentesis-diagnostic-tests>
- <sup>38</sup> Maxwell-Otungo, K (2002) *Towards a communication strategy for the NHS Sickle Cell & Thalassaemia Screening Programme. A planning framework based on preliminary community consultation.* <https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-community-outreach-research>

# Chapter 5 - Counselling and Referral for Prenatal Diagnosis

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## 5.1 Introduction

This guidance has been prepared for healthcare professionals who provide counselling and referral for prenatal diagnosis (PND) to couples/women at risk of having a baby with sickle cell disease or thalassaemia major.

Couples/women at risk are defined as:

- both biological parents are carriers of a significant haemoglobin gene variant
- the woman is a carrier of a significant haemoglobin gene variant and the screening status of the biological father is unknown

If it is not possible to test the baby's biological father in every pregnancy and a previous result is being used then this fact must be recorded in the woman's notes for the current pregnancy.

The previous result must be from a laboratory accredited by the UK Accreditation Service (UKAS), and be consistent, unequivocal, well documented and interpreted and reported within the algorithms of the [laboratory handbook](#).

All maternity units should provide a publically available and advertised direct dial number and/or email address for the use of women, GPs and midwives. There must be a clear pathway, with a named individual or team responsible at each step to:

- provide direct access to counselling and PND for known at risk couples/known carrier women
- check screening results
- offer testing to the baby's biological father
- identify women and couples at risk of having a baby with sickle cell disease or thalassaemia major in their current pregnancy
- counsel women/couples and refer for PND
- obtain the fetal sample and dispatch to the molecular laboratory along with parental venous blood samples
- follow up after PND

A flow chart outlining the pathway is in Appendix 7.

## 5.2 Carrier women and at risk couples

Carrier women with no paternal result available, and known carrier couples, who are “*at risk*” of having a baby with a major haemoglobin disorder must be:

- offered an urgent face to face counselling appointment to explain their carrier status, and given information about the condition that may affect their baby (a sample counselling form is in Appendix 6)

- made aware that in pregnancies that result from egg or sperm donation, the genes inherited by the baby are those of the biological donor
- provided with an explanatory leaflet<sup>39</sup> either before, or after the counselling session
- given information regarding the options for the pregnancy
- given contact details of UK patient societies for the relevant condition ([SCS](#) or [UKTS](#))
- made aware that the decision to have a diagnostic test is an informed choice by the woman/couple
- offered an appointment for PND
- made aware of the intrinsic miscarriage risk associated with PND whether the baby is affected or not<sup>40; 41</sup>

### 5.3 Women and couples who present as known carriers

Women/couples with carrier status known prior to the current pregnancy must be fast-tracked and immediately offered a counselling appointment to discuss their options for the pregnancy **as soon as they present in pregnancy**. Confirmatory carrier screening must still be offered to the couple. To avoid delay in access to PND this **should occur at the same time** as the referral.

If the baby's biological father is unavailable for screening in this pregnancy, then the woman should still be counselled and offered PND without a paternal screening result. A [risk assessment](#) based on the ethnicity of the baby's father is required to determine the risk of him being a carrier.

### 5.4 Referral for prenatal diagnosis

If there is any doubt about the parental genotypes, or the need for further parental testing prior to fetal sampling, contact the relevant molecular haemoglobinopathy laboratory for advice.

There are four haemoglobinopathy DNA laboratories in England which offer analysis of prenatal diagnosis samples for sickle cell disease and thalassaemia disorders.<sup>42; 43</sup> Each laboratory has their own specified prenatal diagnosis request form, and a fully completed form must accompany the fetal and parental samples. Please see Appendix 5 for further details.

The following details, in addition to demographic information for both parents, must be included on the PND referral form:

- maternal and paternal (if available) haemoglobinopathy results
- gestational age of the fetus including EDD by LMP
- maternal antenatal screening booking blood results (where feasible; do not delay the referral);
  - full blood count
  - Hepatitis B status
  - HIV status
  - blood group and rhesus factor
- whether the woman/couple consent to PND for any other condition, such as Fetal Anomaly



## 5.5 Parental samples

A parental blood sample (10 ml EDTA from each parent), must be sent to the DNA laboratory with the fetal sample, regardless if the woman/couple have had a previous PND.

If a paternal sample is unavailable, a maternal blood sample should still be sent to confirm the maternal genotype and to exclude maternal contamination of the fetal sample.

If the paternal genotype is

- **known** (i.e. the father has been previously tested) but he is unavailable or declines testing; then a copy of his laboratory result should be sent to the prenatal diagnosis laboratory so that the fetal risk can be assessed. The result should be from a laboratory accredited by UKAS, and be consistent, unequivocal and well documented.
- **unknown** and he is unavailable or declines testing, PND can still be carried out but this makes diagnosis of conditions more complex. If extended testing is required, this could delay the turnaround time of the fetal diagnosis. If the ethnic origin of the father is known, this should be included on the PND referral form.

## 5.6 Sickle cell disease

Fetal diagnosis of a haemoglobin disorder in the case of sickle cell disease is generally a straightforward process, and is usually achieved without the need for molecular confirmation of parental carrier status.

## 5.7 Thalassaemia conditions

In thalassaemia conditions it is possible to inherit one of a large range of genetic mutations. If a couple have not had PND before, send parental bloods for molecular confirmation of carrier status prior to fetal sampling. This will assist with a quicker fetal diagnosis result. If the couple has had PND before, or molecular confirmation, details of the previous PND should be included on the referral form.

## 5.8 Declining prenatal diagnosis

If PND is declined the healthcare professional who has counselled the couple and recorded their decision, must inform:

- parents of the process for screening their baby after birth and how they will obtain the result
- the maternity department screening coordinator or equivalent
- the woman's GP
- the newborn screening laboratory of the "at risk" couple (see Appendix 3 for an example of a pregnancy alert form)
- the couple of contact details for UK patient societies for the relevant condition

## 5.9 Prenatal Diagnosis: The Procedure

Local arrangements must be in place to obtain an urgent fetal sample for prenatal diagnosis. The diagnostic approach<sup>41; 44</sup> usually depends on the gestational age of the fetus, and the sample will be obtained by one of the following methods:

- **chorionic villus sampling** undertaken from 11 weeks of pregnancy
- **amniocentesis** performed from 15-16 weeks of pregnancy
- **fetal blood sampling** may also be an option

The molecular haemoglobinopathy laboratory must be contacted prior to dispatch of the sample, so that they expect a prenatal diagnosis sample for analysis. This ensures that the failsafe mechanisms to identify samples that do not arrive can be implemented.

## 5.10 Prenatal Diagnosis Follow-up

### Reporting

Prenatal diagnosis results assume that the stated family relationships are true. Any inaccuracies, such as non-paternity, can lead to a misdiagnosis of the fetal condition. Results must be:

- issued within **3 working days** following receipt of the sample in the DNA laboratory
- sent to the named healthcare professional via a secure, confidential method. A copy of the report may also be sent by first class post
- communicated to the woman/couple within 5 working days of the PND test

In special circumstances the final result may be delayed beyond 3 working days, for example

- no paternal sample or genotype
- complicated genetics
- inadequate sample
- maternal contamination of the sample
- multiple pregnancies

### Results

The pathway for giving the woman/couple the results should be agreed during the counselling session prior to the procedure. Clinicians must ensure there are processes in place for all the PND results, including fetal karyotyping, to be communicated to the parents. The report will show one of the following results; not affected, carrier or affected.

If the baby is not affected, or is a carrier then:

- no further appointments or follow up is required during pregnancy. *The pregnancy should continue as normal*
- a record of the results and the baby's due date should be kept by the maternity/specialist counselling service for review after the baby's birth
- the relevant newborn blood spot screening laboratory should be informed of the PND result (a sample notification form is in Appendix 8)
- parental screening and PND results should be included on the newborn blood spot card<sup>45</sup>

If the baby is **affected with a major haemoglobin disorder** and the woman/couple **choose not to** have a termination of pregnancy, then the responsible healthcare professional must:

- offer the woman/couple an opportunity for a face to face discussion about the results
- offer the parents a paediatric consultation to discuss the implications for their baby
- offer counselling
- offer the couple contact details for UK patient societies for the relevant condition
- communicate information about the PND results to all healthcare professionals involved in the ongoing pregnancy
- notify the newborn screening laboratory of the PND result and the fact that the couple are continuing the pregnancy (a sample notification form is in Appendix 7)
- ensure that arrangements are made for parental screening and PND results to be included on the newborn blood spot card.<sup>45</sup>

If the baby is **affected with a major haemoglobin disorder** and the woman/couple consider having a **termination of pregnancy**, an opportunity for a face to face discussion with the relevant healthcare professional(s) should be provided in order to:

- confirm the decision to proceed with a termination of pregnancy
- explain the termination procedure, and what happens afterwards

The PND results and subsequent parental decision must be recorded in the maternity and counselling records and communicated to all relevant healthcare professionals involved in the screening pathway.

Termination of pregnancy should be organised and provided within 5 days of making the decision.<sup>46</sup>

Ongoing counselling support should be offered to the woman/couple by a qualified healthcare professional (HCP).

### 5.11 Termination of pregnancy<sup>47</sup>

Arrangements for termination of pregnancy should be organised locally by the Trust where the pregnancy booking occurred.

The legal limit generally for termination of pregnancy is 24 weeks gestation.<sup>47; 48</sup> However, where the termination of pregnancy is due to a severe fetal abnormality such as a major haemoglobinopathy, this limit on gestation does not apply.<sup>49; 50</sup>

## 5.12 Pre-implantation Genetic Diagnosis<sup>51</sup>

Pre-implantation genetic diagnosis (PGD) enables people with a specific inherited condition in their family to avoid passing it on to their children. It involves checking the genes of embryos created through IVF for specific genetic conditions, avoiding the need for invasive pre-natal diagnostic procedures and possible termination of an affected pregnancy.

The process to establish pregnancy is identical to that used for infertility treatment with the genetic status of embryos pre-determined in vitro using assisted reproductive technology.

Further information is available from <https://www.gov.uk/guidance/sickle-cell-and-thalassaemia-screening-programme-overview>

## 5.13 Data Collection

Annual data on all PNDs performed throughout England is collected and published by the NHS Sickle Cell & Thalassaemia Screening Programme.<sup>52</sup>

In April 2016, the National Congenital and Rare Disorders Registration Service (NCARDS)<sup>53</sup> began collecting national data on PND on behalf of the NHS Sickle Cell & Thalassaemia Screening Programme.

Screening midwives or specialist counselling services are required to complete a pregnancy outcome form for each PND, and return the information to the relevant haemoglobinopathy DNA laboratory, so that a record of the pregnancy outcome can be completed. Each DNA laboratory has modified their form to include their specific details however the Programme has a generic form for reference in Appendix 9.

## 5.14 Websites

- Sickie Cell Society (SCS) <http://sicklecellsociety.org/>
- UK Thalassaemia Society (UKTS) <http://www.ukts.org/>
- Antenatal Results & Choices (ARC) <http://www.arc-uk.org/for-parents/publications-2>
- The Miscarriage Association [www.miscarriageassociation.org.uk](http://www.miscarriageassociation.org.uk)
- Modell's Haemoglobinopathologist's Almanac <http://www.modell-almanac.net/>
- National Congenital Anomaly and Rare Disease Registration Service (NCARDS) <https://www.gov.uk/guidance/the-national-congenital-anomaly-and-rare-disease-registration-service-ncards>
- NHS Sickie Cell & Thalassaemia Screening Programme <https://www.gov.uk/guidance/sickle-cell-and-thalassaemia-screening-programme-overview>
- Royal College of Obstetricians & Gynaecologists (RCOG) <https://www.rcog.org.uk/>
- UK Genetics Testing Network (UKGTN) <http://ukgt.nhs.uk/>

## 5.15 References

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- <sup>39</sup> NHS Sickie Cell & Thalassaemia Screening Programme (2015) *Information for couples "at risk" of having a baby with sickie cell disease or thalassaemia major* <https://www.gov.uk/government/publications/baby-at-risk-of-having-sickle-cell-disease-description-in-brief> and <https://www.gov.uk/government/publications/baby-at-risk-of-having-thalassaemia-description-in-brief>
- <sup>40</sup> Royal College of Obstetricians & Gynaecologists (2011) *Chorionic villus sampling and amniocentesis* <https://www.rcog.org.uk/en/patients/patient-leaflets/amniocentesis-and-chorionic-villus-sampling/>
- <sup>41</sup> Public Health England (2017) *CVS and amniocentesis diagnostic tests: description in brief* <https://www.gov.uk/government/publications/cvs-and-amniocentesis-diagnostic-tests-description-in-brief>
- <sup>42</sup> UK Genetics Testing Network <http://ukgt.nhs.uk/find-a-test/search-by-laboratory/laboratory/>
- <sup>43</sup> NHS Sickie Cell & Thalassaemia Screening Programme (2017) *Handbook for Antenatal and DNA Laboratories 4<sup>th</sup> Edition* <https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-handbook-for-laboratories>
- <sup>44</sup> Royal College of Obstetricians & Gynaecologists (2010) *Amniocentesis and Chorionic Villus Sampling (Green-top Guideline No.8)* <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg8/>
- <sup>45</sup> Newborn Bloodspot Screening Programme (2016) *Guidelines for newborn blood spot sampling* <https://www.gov.uk/government/publications/newborn-blood-spot-screening-sampling-guidelines>
- <sup>46</sup> UK Thalassaemia Society (2016) *Thalassaemia Standards* <http://ukts.org/standards/Standards-2016final.pdf>
- <sup>47</sup> Government Legislation (1967) *Abortion Act 1967 (including updates in force on or before 17<sup>th</sup> November 2016)* <http://www.legislation.gov.uk/ukpga/1967/87/contents>
- <sup>48</sup> Royal College of Obstetricians & Gynaecologists (2011) *The care of women requesting induced abortion (Evidence-based Clinical Guidance #7)* <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/the-care-of-women-requesting-induced-abortion/>
- <sup>49</sup> Letter from the Chief Medical Officer (February 2012) *Letter to all those involved in providing and commissioning treatment for termination of pregnancy.* <https://www.gov.uk/government/publications/abortion-act-1967-as-amended-termination-of-pregnancy>
- <sup>50</sup> Royal College of Obstetricians & Gynaecologists (2010) *Termination for Fetal Abnormality in England, Scotland & Wales* <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/termination-of-pregnancy-for-fetal-abnormality-in-england-scotland-and-wales/>
- <sup>51</sup> Genetic Alliance *Pre-implantation Genetic Diagnosis* <http://www.geneticalliance.org.uk/information/services-and-testing/preimplantation-genetic-diagnosis-information-for-patients>

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<sup>52</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2017) *Data report, trends and performance analysis* <https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-data-trends-and-performance-analysis>

<sup>53</sup> National Congenital Anomaly and Rare Disease Registration Service <https://www.gov.uk/guidance/the-national-congenital-anomaly-and-rare-disease-registration-service-ncards>

# Chapter 6 Antenatal screening - Special circumstances

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## 6.1 Adoption

If either biological parent is adopted, they may not have accurate information on their true family origins. In low prevalence (LP) areas, these individuals should be treated as high risk and the woman should have full laboratory screening.

## 6.2 Women with relevant medical conditions or treatment who book for antenatal care

### 6.2.1 Blood transfusion

Individuals who have had a recent blood transfusion, present misleading data on screening tests, and will not show a true haemoglobinopathy result. During booking for antenatal care ask **all** women if they have ever had a blood transfusion and if they have, then the healthcare professional (HCP) should record

- why did they have a blood transfusion?
- when was the last transfusion?
- where did they/do they have transfusions?

This information should also be conveyed to the laboratory on the blood test or [Family Origin Questionnaire](#) (FOQ) form.

### 6.2.2 Bone marrow transplant

If either biological parent has had a bone marrow (BMT) or stem cell transplant, the haemoglobinopathy screen results will usually reflect the BMT donor. This means that the genetic risk to the fetus will not be clearly identified.

If the biological mother has had a BMT, the baby's biological father must be tested to ensure that this is not a high risk pregnancy. If confirmation of the biological mother's or father's status is required, then a DNA test will be needed. Follow up should be based on both parental results.

### 6.2.3 Woman with a major haemoglobin disorder

Pregnant women who have a major haemoglobin disorder are considered “high risk” and should always be booked for joint obstetric/haematologist care antenatally and not for midwifery-led care. The HCP responsible for following up screening results should ensure that joint care by Obstetrician and Haematologist is initiated.

Occasionally antenatal screening may identify women with previously undiagnosed sickle cell disease (Hb SC; Hb S/Beta<sup>+</sup> Thalassaemia). However, the majority of women with sickle cell disease and all women with thalassaemia major will know they have a condition before they become pregnant. HCPs need to be aware that:

- there is a higher risk of having a baby with sickle cell disease or thalassaemia major (2 in 4 or 50% chance) if the baby’s father is a carrier
- the woman should be offered an appointment for counselling regarding care of her condition during pregnancy, as well as for genetic counselling and screening of the baby’s biological father
- if the woman is being transfused, blood tests may show normal or carrier status, and a careful booking history is required to identify the fact that the woman has a major haemoglobin disorder
- even if the woman has had a bone marrow transplant she will be “cured” of the condition but can still pass a haemoglobinopathy gene on to her children
- the woman with a major haemoglobin disorder requires specialist care during pregnancy and increased clinic visits may be indicated. The woman and baby require close monitoring and a hospital delivery should always be booked

Guidance on care of pregnant women with [sickle cell disease](#)<sup>54</sup> or [thalassaemia major](#)<sup>55</sup> can be accessed on the Royal College of Obstetricians and Gynaecologists website, and in the Programme Centre’s [eLearning](#) Module, Units 3 and 4.

### 6.3 Women who book late in pregnancy or present un-booked in labour

Women who book very late in pregnancy, or who show up at the maternity unit in labour, must be offered screening for a haemoglobinopathy. If she is in labour then this could be in either the intra or post-partum period.

Results should be obtained within 3 working days, and the offer of paternal screening should be conducted in the same way as for routine antenatal screening early in pregnancy.

Although the focus here is not reproductive choice or the option to have prenatal diagnosis in this pregnancy, it is important the woman’s knows her genotype

- for her personal health
- in preparation for newborn screening
- for future pregnancies



## 6.4 Screening results following miscarriage or termination of pregnancy

If a woman is screened antenatally and then has a miscarriage or abortion, she must still be

- informed of her screening results
- provided with an [information leaflet](#) about her carrier status (where relevant)
- offered counselling and partner screening if she is a carrier

## 6.5 Woman with a haemoglobinopathy who does not attend or cancels counselling appointment (DNA)

Some women may not attend for antenatal genetic counselling following a positive or inconclusive screening result. There must be a local policy in place to ensure that the woman receives information about

- her haemoglobinopathy screening result
- her specific [carrier](#) status (as appropriate)
- how to contact the HCP for counselling at a later date if she changes her mind

Primary care services and the community midwife should also be informed of the woman's result, and her non-attendance for genetic counselling and screening of the baby's biological father.

## 6.6 Couples with assisted pregnancies<sup>56</sup>

### Fertility treatment with sperm or egg donation or surrogacy

If a woman has had **fertility treatment** then it is important to establish the source of both egg and sperm to assess the potential risk of the baby inheriting a haemoglobin disorder. If both egg and sperm are from the baby's biological parents, then the risk to the baby can be assessed as for any other carrier woman/couple.

If the sperm or the egg has been donated to the couple, then it is not possible to do a risk assessment of the pregnancy based on the parental screening results. If the donor sperm and/or egg have been screened for a haemoglobinopathy and the results are available then this can be discussed with the couple.

If pregnancy has been achieved through a **donor egg** then the screening results on the woman will not be informative. Even if she is not the baby's biological parent, it is best practice to always test the pregnant woman for a haemoglobinopathy, to ensure optimal maternal care during pregnancy. The

baby's biological father must also be tested, irrespective of the woman's result and, if screen positive, the fertility clinic should be contacted to obtain the biological mother's haemoglobinopathy results.

If **donor sperm** has been used and the mother has a positive screening result then, where possible, the fertility clinic should be contacted to obtain the biological father's haemoglobinopathy results.

In the case of **surrogacy**<sup>57</sup> the fertility clinic should be contacted to obtain the haemoglobinopathy results of both biological parents.

If no screening results are available for either donor sperm or egg then the process for dealing with this situation should be locally determined with discussions between maternity services, specialist nurses and consultant haematologist.

## 6.7 Linkage between antenatal and newborn screening

The linked NHS Sickle Cell and Thalassaemia Screening programme is delivered across professional and organisational boundaries and clear pathways and robust partnerships are required. The linked programme encourages practitioners to review results from antenatal testing before, during and after the newborn screening test is offered and to check that the results are congruent.

At a minimum, all maternal carrier results, and all at risk couple results should be linked to the appropriate newborn screening results. A form to facilitate this link has been developed (Appendix 8).

Maternal and paternal (where available) antenatal screening results should be recorded on the newborn screening bloodspot card.

A linked service:

- makes sure that every step of the screening process is informed by results from the previous step
- allows more accurate interpretation of the newborn screening results, avoiding unnecessary repeat testing, if both the maternal and paternal results are known
- allows parents who have been screened antenatally to have prior information regarding the risk of their baby inheriting a condition, or being a carrier, and allows them to be prepared
- can help ensure that everyone's results are accessible throughout their lifetime, so that the appropriate information and care can be provided when and where it is needed.

A linked service does not always contribute to reducing parental anxiety. If the mother's antenatal results show normal haemoglobin then the father will not generally have been

tested. If the baby is subsequently found to be a carrier, the risk would not have been identified antenatally. Research shows that prior knowledge of carrier status gives parents a more positive newborn screening experience than discovering test results out of the blue.<sup>58</sup>

The antenatal report given to all women following the birth of their baby should contain all antenatal screening results, including sickle cell and thalassaemia screening, for communication to primary care.

## 6.8 Guidance concerning possible non-paternity

All genetic tests undertaken during pregnancy and the newborn period, will include the possible issue of non-paternity. This needs to be considered by all HCPs when offering screening tests, and when inviting the 'baby's father' for testing. It should be highlighted to the mother that the correct person to be screened is the 'baby's biological father' in order to assess the genetic inheritance in the baby correctly.

The role of HCPs is to provide clarity and discretion around genetic screening test results, particularly as there is no consensus on the rate of non-paternity in the population.<sup>59</sup> Obtaining this unsolicited information during screening creates an ethical dilemma about whether to pass the information on, and to whom. The revelation of non-paternity may be detrimental to established relationships and HCPs must be alert to the need for discretion in pursuing family studies and in discussing results with the mother/parents.

Non-paternity may be suspected when<sup>60</sup>

- a baby with a major haemoglobin disorder has a carrier mother but the 'father' is not a carrier
- a baby identified as a carrier has neither their mother nor their father identified as a carrier

However, even when screening results seem to suggest non-paternity, alternative explanations must also be considered, for example:

- one parent may carry a variant that cannot be detected by routine screening methods, e.g. an unstable variant or a silent form of beta thalassaemia
- there may have been an error
  - a) with labelling a sample
  - b) in the laboratory
  - c) or in reporting the results
- a parent's identity may have been stolen or used by another person
- the couple may have used assisted reproductive methods (artificial insemination by donor egg/sperm), which may not have been declared
- a very premature baby may not yet have developed any of their adult haemoglobin
- the baby may have developed a De Novo mutation, which although rare, is possible

Despite these possibilities, a risk of non-paternity remains and needs to be handled carefully if relationships and family units are not to be disrupted. When discussing results the need for discretion is essential.

The HCP needs to be non-judgemental while considering the following actions:

- 1) review the antenatal and newborn screening process to establish whether or not an error may have occurred at any stage of the pathway
- 2) explore the possibility of non-paternity with the mother, preferably on her own in private, without her partner present
- 3) agree with the baby's mother how the situation will be dealt with if non-paternity is indeed a possibility
- 4) offer a re-test (in the first instance) to:
  - a) mother
  - b) baby
- 5) if indicated, re-screen the father
- 6) carefully document results and communicate these only to those HCPs who need the information to support the family.

## 6.9 References

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<sup>54</sup>-Royal College of Obstetricians and Gynaecologists (2011) *Sickle Cell Disease in Pregnancy, Management of* (Green-top Guideline 61) Reviewed December 2014  
<https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg61/>

<sup>55</sup> Royal College of Obstetricians and Gynaecologists (2014) *Thalassaemia in Pregnancy, Management of Beta* (Green-top Guideline 66) <https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg66/>

<sup>56</sup> Human fertility and embryology authority *Fertility treatments* <https://www.hfea.gov.uk/treatments/>

<sup>57</sup> Human fertility and embryology authority <https://www.hfea.gov.uk/treatments/explore-all-treatments/surrogacy/>

<sup>58</sup>Kai, J Ulph, F Cullinan, T and Qureshi, N (2009) Communication of carrier status information following universal newborn screening for sickle cell disorders and cystic fibrosis: qualitative study of experience and practice. *Health Technology Assessment* 2009; Vol. 13: No. 57 [www.hta.ac.uk](http://www.hta.ac.uk)

<sup>59</sup>Voracek M; Haubner T; Fisher ML (2008) Recent decline in nonpaternity rates: a cross-temporal meta-analysis. *Psychological Rep.* 2008 Dec; 103(3): 799-811

<sup>60</sup>Turney L (2005) The Incidental Discovery of Non-paternity Through Genetic Carrier Screening: An Exploration of Lay Attitudes. *Qualitative Health Research* 2005; 15(5): 620

# Chapter 7 - Newborn Screening

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Newborn screening (NBS) is offered as part of the [newborn blood spot \(heel prick\) test](#)<sup>61</sup> and identifies babies who have sickle cell disease. It also detects babies who are genetic carriers of some haemoglobin variants. The key reason for offering newborn screening is that babies with sickle cell disease are vulnerable to life-threatening infections. By identifying them promptly after birth, they can be offered potentially life-saving penicillin, and be referred for specialist care.

There is no routine screen for babies at risk of inheriting thalassaemia major - although this is currently under review. However, most cases of beta thalassaemia major should be detected during newborn screening, but beta thalassaemia carriers are not.

Newborn bloodspot screening is performed on day 5 of birth, counting the day of birth as day 0. Additionally, babies up to 12 months of age who become the responsibility of the provider organisation must be offered screening if there is no documented evidence of a conclusive result for the conditions currently recommended by the UK National Screening Committee (UK NSC).

The [SCT](#)<sup>62</sup> and [NBS](#)<sup>63</sup> screening programmes have published standards for newborn screening, against which screening services will be assessed and monitored.

## 7.1 Linked antenatal and newborn screening programme

Linking the results of the parents and the babies is particularly important for the sickle cell and thalassaemia screening programme as it helps to make an accurate diagnosis in the baby.

All maternal carrier results, and at risk couple results, should be linked to the appropriate newborn screening results.

There is a notification form that should be used to inform newborn blood spot screening laboratories of any carrier women and at risk couples (Appendix 8).

## 7.2 Offer of the newborn blood spot screen

Parents must be offered information about the newborn blood spot screen prior to the offer of screening. The parent's information leaflet '[Screening tests for you and your baby](#)'<sup>64</sup> is available to support information from a healthcare professional. The leaflet is available in a number of languages and an easy read version.

Full guidance on performing the NBS is covered in the Newborn Blood Spot Screening guidelines.<sup>65</sup>

If the screen is accepted:

- it should be recorded in the maternity record and the Personal Child Health Record (PCHR).
- if the baby is in hospital then the consent should also be recorded in the baby's hospital records.

If the screen is declined:

- this should be recorded on the bloodspot card and sent to the laboratory
- each condition for which this is relevant, must be recorded in the maternity records and the PCHR
- the baby's GP and health visitor must be informed of the conditions for which the parents have declined screening
- the parents should be informed that the baby can be screened at a later date if they so wish

### 7.3 Babies born to “at risk” couples

Couples at risk of having a baby with a major haemoglobin disorder, where the results of both parents are known, may wish to know their baby's result before the normal time for reporting from bloodspot screening.

Local policies should be in place to have an early newborn bloodspot test, at the parents' request. Alternately, a liquid capillary blood specimen (not cord blood) can be taken for analysis soon after birth. This is not part of the screening programme, and should be considered as an aspect of parental choice.

The blood sample must be analysed in a laboratory which has expertise in haemoglobinopathy analysis in the newborn period. Please refer to the [Handbook for Newborn Laboratories](#)<sup>66</sup> for further details.

### 7.4 Preterm babies

Preterm babies or those in neonatal units:

- require the sample to be taken on day 5
- would benefit from the coordination of the NBS with other blood tests to minimise discomfort

Be aware that preterm babies do not always show their adult haemoglobin clearly, depending on their gestational age.

### 7.5 Transfused babies

Babies that require a blood transfusion must have a NBS for sickle cell taken prior to the blood transfusion.

The pre-transfusion sample must be clearly labelled 'pre-transfusion' on the blood spot card. The remaining conditions are to be screened on day 5 on a separate blood spot card, as routine. Both cards must then be submitted together to the newborn screening laboratory.

In the cases when a baby has had a blood transfusion before a pre-transfusion sample has been taken, it is possible to perform DNA testing on post-transfusion samples. The DNA test will detect the presence of the sickle haemoglobin gene. The test is able to differentiate between babies with:

- only the sickle gene present
- those with the sickle gene and another globin gene (either a normal beta gene or another variant)
- no sickle gene present

If the sickle gene is detected the baby must be referred for clinical follow up. Please see Appendix 10 for further information.

## 7.6 Newborn screening results

### Screen negative

Approximately 97% of babies will be screen negative. This means the baby is unaffected or none of the haemoglobin variants that must be identified have been detected. The parents should be informed before the baby's health check at 6-8 weeks.

### Haemoglobin variant carrier

Approximately 9000 babies every year in England are found to be a healthy carrier of a haemoglobin gene variant. This is a prevalence of one in 70 [births](#).<sup>67</sup>

The haemoglobin gene variants the NBS screening must identify are:

Hb S

Hb C

Hb D

Hb E

Hb O<sup>Arab</sup> (additional investigations are required to confirm this result).

The results will show the presence of HbF, Hb A and the haemoglobin variant

It is important for parents to understand that their child could pass on the gene for unusual haemoglobin to future generations.

The parents of babies found to be carrier of a haemoglobin gene variant must be given the opportunity for a face to face discussion with a suitably [trained](#) professional to enable the significance of the carrier status to be explained. It is important for the parents to understand that their child could pass on the gene for unusual haemoglobin to future generations when they have their own baby.

There are 2 parent information leaflets to support the information given by a healthcare professional:

[Information for mums and dads: your baby carries a gene for sickle cell](#)<sup>68</sup>

[Information for mums and dads: your baby carries a gene for unusual haemoglobin](#)<sup>69</sup>

Both leaflets are available in English, French, Bengali and Urdu.

It is important to remember that it is not possible to identify those babies that are beta thalassaemia carriers, using routine newborn screening methods.

### Inconclusive results

For babies found to have a haemoglobin variant other than those stated above, the NBS result will be issued as 'condition not suspected'. The wording will state that haemoglobin S, C, D<sup>Punjab</sup>, E, and O<sup>Arab</sup> have not been detected

## 7.7 Benign haemoglobin conditions

There are a number of benign haemoglobin conditions that may be detected in the NBS. In such cases, the baby should be referred to a named clinician for follow up and counselling. There may be an indication to rescreen these babies. Please see appendix 2 for further details of the conditions below.

Benign haemoglobin conditions include:

Hb CC and C/ $\beta$ thalassaemia

Hb DD and D/ $\beta$ thalassaemia

Hb CD

Hb CE

Hb DE

Hb EE

## 7.8 Baby has sickle cell disease

Results from babies with sickle cell disease show the presence of HbF and HbS in the absence of HbA; or HbF and HbS with another haemoglobin variant. Between 260-350 babies a year in England have a sickle cell disease result; this is a prevalence of one per 2,000-2,500 births.

Expected results from babies with sickle cell disease are:

Newborn screening result	Disease
FS	Hb SS
FS	Hb S/ $\beta^0$ thalassaemia
FS	Hb S/ $\delta\beta$ thalassaemia
FS	Hb S/Lepore



<b>FS</b>	<b>Hb S/HPFH</b>
<b>FSA or FS</b>	<b>Hb S/<math>\beta^+</math> thalassaemia</b>
<b>FSC</b>	<b>Hb SC</b>
<b>FSD</b>	<b>Hb S/D<sup>Punjab</sup></b>
<b>FSE</b>	<b>Hb S/E</b>
<b>FSO<sup>Arab</sup></b>	<b>Hb S/O<sup>Arab</sup></b>

The parents of babies who have a sickle cell disease result from the NBS must be informed of the result before the baby is 28 days of age. This is an auditable [standard](#)<sup>63</sup> in the sickle cell and thalassaemia screening programme.

The parents must be informed by an appropriately [trained](#) professional, with sensitivity to the parents' concerns. Best practice is for the parents to be informed by a healthcare professional they have met in the antenatal period, along with either the family's health visitor or a haemoglobinopathy paediatric nurse. The family must be given contact numbers, and all relevant healthcare professionals informed of the result.

The early identification of affected babies allows:

- the opportunity to inform and educate the parents of the condition
- early intervention to reduce morbidity and mortality
- prophylactic oral penicillin v to be commenced
- timely entry into specialist haemoglobinopathy centre

The standard is for affected babies to attend a haemoglobinopathy centre (medical) by 90 days of age.

There is a [parent information book](#)<sup>70</sup> available which gives detailed guidance on to have to care for an affected child. This can be obtained from [Harlow Press](#).

An example of a form which could be used to support the counselling session, and also as a template of a referral letter is in Appendix 10.

Appendix 3 has further details of the clinical impact of each sickle cell disorder.

## 7.9 Beta thalassaemia

The NBS programme does not specifically screen for beta thalassaemia major, but babies with severe thalassaemia major will generally be detected. Results from a baby with severe Beta thalassaemia major will usually have only HbF present and no HbA. It is important to remember that not all thalassaemia conditions will be detected by the NBS.

Babies with a Beta thalassaemia condition must be referred for follow up and care to a haemoglobinopathy centre (medical) by 90 days of age.

It is important to remember that it is not possible to identify those babies that are beta thalassaemia carriers. Parents should be informed of this in the antenatal period if relevant.

## 7.10 Non-Paternity

Healthcare professionals involved in newborn screening must be mindful that there is the potential for the results to identify possible non-paternity of the baby. Such cases must be handled sensitively.

Further information is available in Chapter 6 of the programme handbook.

## 7.11 References

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<sup>61</sup> NHS Newborn Blood Spot Screening Programme (2017) *Programme Overview*

<https://www.gov.uk/topic/population-screening-programmes/newborn-blood-spot>

<sup>62</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2017) *Sickle cell & thalassaemia screening: programme standards* <https://www.gov.uk/government/publications/standards-for-sickle-cell-and-thalassaemia-screening>

<sup>63</sup> NHS Newborn Blood Spot Screening Programme (2017) *Newborn blood spot screening programme standards* <https://www.gov.uk/government/publications/standards-for-nhs-newborn-blood-spot-screening>

<sup>64</sup> Public Health England (2017) *Screening tests for you and your baby.*

<https://www.gov.uk/government/publications/screening-tests-for-you-and-your-baby-description-in-brief>

<sup>65</sup> NHS Newborn Blood Spot Screening Programme (2016) *Newborn blood spot screening: sampling guidelines* <https://www.gov.uk/government/publications/newborn-blood-spot-screening-sampling-guidelines>

<sup>66</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2017) *Handbook for newborn laboratories* <https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-handbook-for-laboratories>

<sup>67</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2017) *Sickle cell and thalassaemia screening: data trends and performance analysis* <https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-data-trends-and-performance-analysis>

<sup>68</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2016) *Baby carries a gene for sickle cell: description in brief*

<https://www.gov.uk/government/publications/baby-carries-a-gene-for-sickle-cell-description-in-brief>

<sup>69</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2010) *Baby carries a gene for unusual haemoglobin: description in brief* <https://www.gov.uk/government/publications/baby-carries-a-gene-for-unusual-haemoglobin-description-in-brief>

<sup>70</sup> NHS Sickle Cell & Thalassaemia Screening Programme (2012) *A parent's guide to Sickle cell disease* <https://www.gov.uk/government/publications/sickle-cell-disease-managing-the-condition>

# Chapter 8 - Failsafe, Quality Assurance and Data Collection

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Each NHS screening programme has a defined screening pathway<sup>71</sup>

The NHS Sickle Cell and Thalassaemia Programme has a [second pathway](#) for known at risk women and couples.

The pathways show how the individual undergoing screening moves from one stage of the pathway to the next. [Checks](#) are needed at each stage to ensure the individual moves seamlessly and safely through the pathway unless they choose not to.

If these checks are not in place there is a risk that an individual does not complete the pathway or the pathway is delayed unnecessarily. Quality assurance of screening programmes includes checking these procedures are in place and operating effectively.

In screening programmes these checks and failsafe processes are in place to ensure if something goes wrong it can easily be identified at the time it goes wrong and action can be taken to correct it before any harm occurs. [Guidance](#)<sup>72</sup> is given by the SCT programme; an [audit template](#)<sup>72</sup> is also available.

## 8.1 Newborn blood spot [failsafe](#)<sup>73</sup> solution (NBSFS)

The NBSFS is in use by maternity units across England. It identifies babies who have missed newborn blood spot (NBS) screening. This enables screening to be offered and affected babies to be identified early and treatment can be started within an effective timeframe.

## 8.2 Quality Assurance

The [screening quality assurance services](#) (SQAS)<sup>74</sup> is the process of checking that national standards are met (ensuring that screening programmes are safe and effective) and encouraging continuous improvement.

All maternity services in England are required to submit quarterly [Key Performance Indicators](#)<sup>75</sup> (KPIs) to the national screening programmes to demonstrate performance against set standards.

Each screening programme provider must report KPI data using the appropriate reporting template. Service users, programme teams and the screening quality assurance service (SQAS) use KPIs to help measure the success of screening programmes.

Maternity services are also subject to peer review, led and supported by the SQAS.

It is important that any screening incidents are managed in accordance with [national guidelines](#)<sup>76</sup>. Incidents must be reported via the local incident reporting systems and to the relevant SQAS team.

### 8.3 Data collection

The sickle cell and thalassaemia programme collects [data](#)<sup>77</sup> to evaluate the delivery of the programme using data from a variety of sources.

The [data report](#)<sup>78</sup> is produced annually and reports performance against antenatal and newborn sickle cell and thalassaemia screening programme standards and trends over time.

### 8.4 References

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<sup>71</sup> Public Health England (2015) *NHS population screening: care pathways*  
<https://www.gov.uk/government/collections/nhs-population-screening-care-pathways>

<sup>72</sup> NHS sickle cell and thalassaemia screening programme (2017) *SCT checks and audit*  
<https://www.gov.uk/government/publications/sct-checks-and-audits-to-improve-quality-and-reduce-risks/sct-checks-and-audits>

<sup>73</sup> NHS Newborn blood spot screening programme (2016) *Newborn blood spot screening: failsafe procedures*  
<https://www.gov.uk/government/publications/newborn-blood-spot-screening-failsafe-procedures>

<sup>74</sup> NHS population screening programmes (2016) *NHS population screening: quality assurance*  
<https://www.gov.uk/guidance/nhs-population-screening-quality-assurance>

<sup>75</sup> NHS Population screening programmes (2017) *Key performance indicators*  
<https://www.gov.uk/government/publications/nhs-population-screening-reporting-data-definitions>

<sup>76</sup> NHS Population screening programme (2015) *Managing safety incidents in NHS screening programmes*  
<https://www.gov.uk/government/publications/managing-safety-incidents-in-nhs-screening-programmes>

<sup>77</sup> NHS Sickle cell and thalassaemia screening programme (2017) *Sickle cell and thalassaemia screening: data collection* <https://www.gov.uk/government/collections/sickle-cell-and-thalassaemia-screening-data-collection>

<sup>78</sup> NHS Sickle cell and thalassaemia screening programme (2017) *Sickle cell and thalassaemia screening: data trends and performance analysis* <https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-data-trends-and-performance-analysis>

# Chapter 9 - Resources & Training

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## Laboratory support service

The NHS Sickle Cell &Thalassaemia Screening Programme funds a support service via Oxford University Hospitals, for HCPs working in the antenatal and newborn screening programmes. There is a designated telephone helpline and secure email address for questions about screening policy and haemoglobinopathy results.

## Contact details

Telephone: 01865572767

Email: [lab.support@nhs.net](mailto:lab.support@nhs.net)

Fax: 01865 572 775

## NHS Sickle Cell &Thalassaemia Screening Programme enquiries

Telephone: 020 3682 0890

Email: [phe.screeninghelpdesk@nhs.net](mailto:phe.screeninghelpdesk@nhs.net)

Website: [gov.uk/phe/screening](http://gov.uk/phe/screening)

## Training Courses & Resources

Kings College London offers 3 courses:

- [Genetic risk assessment](#) (this is a 4 day course for health professionals involved in counselling women and couples 'at risk' of having a child with a haemoglobinopathy)
- [Specialist Counsellors Update](#) (this is a one day update for practitioners who have previously undertaken a specialist course)
- [SCT Screening Programme Update](#) (this is a one day update for non-specialist nurses, midwives and health visitors so that they can develop an understanding of the antenatal and newborn sickle cell and thalassaemia screening programme in England)

[Warwick](#) Health Screening Module

NHS Sickle Cell &Thalassaemia Screening Programme

Core [competencies](#) in genetics for sickle cell and thalassaemia counselling

Other Training Tools

[Sickle Cell Society Family Legacy DVD](#)

## Appendix 1 – Haemoglobinopathy Carriers

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
Haemoglobin AA	Normal haemoglobin	None	Normal haemoglobin seen in all populations	No interaction	Not applicable
Alpha ( $\alpha^+$ ) Plus Thalassaemia carrier	<p>This is not clinically significant, although it may resemble iron deficiency anaemia with normal iron serum levels</p> <p>If carrier status is suspected antenatally then no further tests are recommended</p> <p>Not included in the screening programme in England</p>	None	Most common haemoglobinopathy in populations world-wide	<b>Alpha zero thalassaemia</b>	<p><b>Haemoglobin H Disease (Hb H Disease)</b></p> <p>Prenatal diagnosis (PND) is not indicated for this condition</p>
Alpha ( $\alpha^0$ ) Zero Thalassaemia carrier	<p>2 alpha (<math>--/\alpha\alpha</math>) gene deletion</p> <p>Reduced MCV &amp; MCH</p>	Paternal screening if both parents are from a high risk	China (including Hong Kong), Taiwan, Thailand, Cambodia, Laos, Vietnam, Indonesia, Burma, Malaysia, Singapore,	<p><b>Alpha zero thalassaemia</b></p> <p>Offer couple prenatal diagnosis (PND)</p>	<b>Alpha thalassaemia major (Hb Barts Hydrops Fetalis )</b>

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
	<p>May resemble iron deficiency anaemia with normal iron serum levels</p> <p>DNA required to confirm carrier status, as it cannot be diagnosed by routine screening methods</p> <p>Confirmation of carrier status as part of the antenatal screening programme in England is only indicated if both parents are from a high risk group</p>	<p>group</p> <p>Genetic counselling and DNA to confirm carrier status ONLY if results from both parents indicate they may be alpha zero thalassaemia carriers</p>	Philippines, Cyprus, Turkey, Greece, Sardinia, unknown family origins	<p><b>Alpha plus thalassaemia</b></p> <p>(Unlikely to be detected during antenatal screening as it not considered clinically significant)</p>	<p><b>Haemoglobin H Disease (Hb H Disease)</b></p> <p>PND is not indicated for this condition</p>
Beta (β) Thalassaemia carrier	<p>Elevated haemoglobin A<sub>2</sub> Reduced MCV &amp; MCH Reduced production of β (beta) globin chains</p> <p>May be misdiagnosed as iron deficiency anaemia</p> <p>Unless iron deficient, then no supplement required</p> <p>There are a range of β thalassaemia mutations</p>	<p>Genetic counselling &amp; paternal/partner screening is indicated</p> <p>Sometimes requires DNA to confirm carrier status</p> <p>Not diagnosed during routine newborn screening</p>	<p>Mediterranean Middle East South East Asian South Asian (China, Indonesia, Vietnam and other countries in the region) Caribbean African</p> <p>Occurs sporadically in all populations including White British</p>	<p><b>β thalassaemia</b> Offer couple PND</p>	<p><b>βthal/βthal β thalassaemia major or βthalassaemia Intermedia</b></p>
				<p><b>Hb Lepore</b> Assessment by Specialist - Offer PND if indicated</p>	<p><b>Lepore/ βthal May present as Thalassaemia Major or Thalassaemia Intermedia</b></p>
				<p><b>Hb E</b> Assessment by Specialist - Offer PND if indicated</p>	<p><b>E/βthalassaemia may present as Thalassaemia Major or Thalassaemia Intermedia</b></p>

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
				Delta beta ( $\delta\beta$ ) thalassaemia Assessment by Specialist - Offer PND if indicated	$\beta$ thal/ $\delta\beta$ thal May present as Thalassaemia Major or Thalassaemia Intermedia
				O Arab Assessment by Specialist	O <sup>Arab</sup> / $\beta$ thalassaemia is usually similar to Thalassaemia Intermedia
				Hb S Offer PND	S/ $\beta$ thalassaemia



Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
Hb Lepore carrier (Hb A/Lepore)	Red blood cells are usually hypochromic and microcytic  Occasional enlarged spleen	Genetic counselling  Partner screening	Mediterranean (Greek, Italian)	<b>β thalassaemia</b> Assessment by Specialist - Offer PND if indicated	May present as <b>Thalassaemia Major</b> or <b>Thalassaemia Intermedia</b>
				<b>Sickle cell (Hb AS)</b> Assessment by Specialist - Offer PND if indicated	<b>Hb S/Lepore</b>
Delta (δ) Beta (β) thalassaemia carrier (Hb A/δβ thalassaemia)	Red blood cells are usually hypochromic and microcytic  Occasional enlarged spleen  DNA to confirm diagnosis	Genetic counselling  Partner screening	Mediterranean (Greek, Italian)	<b>β thalassaemia</b> Assessment by Specialist - Offer PND if indicated	May present as <b>Thalassaemia Major</b> or <b>Thalassaemia Intermedia</b>
				<b>Sickle cell (Hb AS)</b> Assessment by Specialist - Offer PND if indicated	<b>Hb S/δβ thalassaemia</b>
Hereditary Persistence of Fetal Haemoglobin carrier (Hb A/HPFH)	Usually 2% or less of total haemoglobin in adults  It is not possible to distinguish Hb SS from Hb S/HPFH and S/β <sup>0</sup> thalassaemia in newborn screening	Genetic counselling  Partner screening	Africans Caribbean	<b>Sickle cell (Hb AS)</b> Assessment by Specialist	<b>S/HPFH</b> Does not usually require treatment
Haemoglobin E carrier (Hb AE)	Lysine substituted for glutamic acid, 26 <sup>th</sup> point β globin chain  Red blood cells may be hypochromic and microcytic	Genetic counselling  Partner screening	South East Asia (India, Bangladesh) South Asia (China, Vietnam, Thailand, Indonesia and other countries in the region) Caribbean	<b>β thalassaemia</b> Assessment by Specialist - Offer PND if indicated	<b>E/β thalassaemia may present as Thalassaemia Major or Thalassaemia Intermedia</b>
				<b>Sickle cell (Hb AS)</b> Assessment by Specialist	<b>Hb S/E Disease</b>

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
Haemoglobin D <sup>Punjab</sup> carrier (Hb AD <sup>Punjab</sup> ) also called D <sup>Los Angeles</sup>  Other types of Hb D are not usually clinically significant	Glutamine substituted for glutamic acid, 121 point, β globin chain  Important to identify D <sup>Punjab</sup> from other Hb D's due to clinical interaction with Hb S	Genetic counselling  Partner screening	Indian Pakistan Caribbean  Occurs sporadically in all populations including White British)	Sickle haemoglobin (Hb S)  Offer PND	Hb S/D <sup>Punjab</sup>
Haemoglobin C carrier (Hb AC)	Lysine substituted for glutamic acid, 6 <sup>th</sup> point, β globin chain	Genetic Counselling Partner screening	West African Caribbean	Sickle haemoglobin (Hb S)  Offer PND	Hb S/C Disorder
Hb O <sup>Arab</sup> (Hb AO <sup>Arab</sup> ) carrier  Also known as Hb Egypt	Lysine substituted for glutamine at 121 <sup>st</sup> point of the β globin chain	Genetic counselling  Partner screening	North Africa Saudi Arabia Bulgaria/Eastern Europe Eastern Mediterranean	β thalassaemia Assessment by Specialist	O <sup>Arab</sup> /βthalassaemia usually similar to Thalassaemia Intermedia
				Sickle haemoglobin (Hb S)  Offer PND	S/O <sup>Arab</sup>

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
Sickle Cell Trait/Carrier (Hb AS)	May have intravascular sickling if oxygen tension excessively low (e.g. during anaesthetic)  Possible haematuria  Possible increased risk of urinary infections in pregnancy	Genetic counselling  Partner screening	African Caribbean South East Asians Mediterranean	<b>β thalassaemia</b> Offer PND	<b>S/β thalassaemia</b>
				<b>Hb C</b> Offer PND	<b>Hb S/C Disease</b>
				<b>Hb S</b> Offer PND	<b>Sickle Cell Anaemia (Hb SS)</b>
				<b>Hb D<sup>Punjab</sup></b> Offer PND	<b>Hb S/D<sup>Punjab</sup></b>
				<b>Hb O<sup>Arab</sup></b> Offer PND	<b>Hb S/O<sup>Arab</sup></b>
				<b>Delta beta (δβ) Thalassaemia</b> Assessment by Specialist	<b>Hb S/δβ thalassaemia</b>
				<b>Hb Lepore</b> Assessment by Specialist	<b>Hb S/Lepore</b>
				<b>Hereditary Persistence Fetal Haemoglobin</b> Assessment by Specialist	<b>S/HPFH</b>  Not usually treated but investigations required

Serious Interaction

Less Serious Interaction

Minimal clinical significance

## References

1. Bain BJ (2006) *Other significant haemoglobinopathies*. Haemoglobinopathy Diagnosis, 2<sup>nd</sup> Edition Blackwall Publishing Ltd
2. Brent Sickle Cell & Thalassaemia Centre (2010) *Interpreting Common Haemoglobinopathy Test Results – A Guide for Primary Health Care Professionals*. <http://sickle-thal.nwfh.nhs.uk/>
3. NHS Sickle Cell & Thalassaemia Screening Programme (2012) *Handbook for Laboratories*. 4<sup>th</sup> Edition. <https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-handbook-for-laboratories>
4. Ryan et al on behalf of the British Committee for Standards in Haematology (2010) *Significant haemoglobinopathies: guidelines for screening and diagnosis*. Blackwall Publishing Ltd British Journal of Haematology 149, 35-49 <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2009.08054.x/epdf>

## Appendix 2 – Benign Haemoglobin Disorders

Genotype	Anaemia	Other clinical features	Comments
<b>Haemoglobin C Disease</b>  <b>C/β<sup>+</sup>·Thalassaemia</b>  <b>C/β<sup>0</sup>·Thalassaemia</b>  or <b>Hb CC</b>	Mild haemolytic anaemia	Occasional intermittent abdominal pain  Gallstones  Fatigue  Occasional jaundice  Usually a mild condition   Genetic counselling is essential during pregnancy for parents 'at risk' of having a child with this condition but prenatal diagnosis is not indicated.	<b>Register with haematology/ specialist clinic</b> decision regarding regularity of follow-up is made locally   No regular treatment necessary, only required in relation to symptoms   Genetic counselling and partner testing for individuals with this condition is important as they do not have any normal Hb A genes.
<b>Haemoglobin D<sup>Punjab</sup> Disease</b> <b>Hb D<sup>Punjab</sup>/D<sup>Punjab</sup></b>  <b>D<sup>Punjab</sup>/β<sup>0</sup>·Thalassaemia</b>  <b>D<sup>Punjab</sup>/β<sup>+</sup>·Thalassaemia</b>	Microcytosis  Hypochromia   Hb at lower end of normal	Occasional abdominal pain  Symptoms related to haemolytic anaemia  Gallstones  Fatigue  Occasional jaundice  Iron medication not required unless iron deficient	<b>Register with haematology/ specialist clinic</b> decision regarding regularity of follow-up is made locally   No regular treatment necessary, only required in relation to symptoms   Genetic counselling and partner testing for individuals with this condition is

Genotype	Anaemia	Other clinical features	Comments
		Genetic counselling is essential during pregnancy for parents 'at risk' of having a child with this condition but prenatal diagnosis is not indicated.	important as they do not have any normal Hb A genes
<b>Haemoglobin E Disease</b> <b>(Hb EE)</b>  <b>(Hb E/<math>\beta^0</math>Thalassaemia</b> may be clinically significant, please see information on thalassaemia disorders for further information)	Mild haemolytic anaemia   Hypochromic	Very mild condition  <b>Genetic counselling is essential during pregnancy for parents 'at risk' of having a child with this condition but prenatal diagnosis is not indicated.</b>  Hb EE and Hb E/ $\beta^0$ Thalassaemia will look similar on the initial screening test and further investigations will be needed for the conditions to be differentiated.	<b>Register with haematology/ specialist clinic</b> decision regarding regularity of follow-up is made locally  No regular treatment necessary, only required in relation to symptoms  Common in South East Asian populations.  Genetic counselling and partner testing for individuals with this condition is important as they do not have any normal Hb A genes.

## References

Bain BJ (2006) *Other significant haemoglobinopathies*. Haemoglobinopathy Diagnosis, 2<sup>nd</sup> Edition Blackwall Publishing Ltd

Brent Sickle Cell & Thalassaemia Centre (2010) *Interpreting Common Haemoglobinopathy Test Results – A Guide for Primary Health Care Professionals*.  
<http://sickle-thal.nwlh.nhs.uk/>

NHS Sickle Cell & Thalassaemia Screening Programme (2012) *Handbook for Laboratories. 4<sup>th</sup> Edition.*  
<https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-handbook-for-laboratories>

Ryan et al on behalf of the British Committee for Standards in Haematology (2010) *Significant haemoglobinopathies: guidelines for screening and diagnosis.*  
Blackwell Publishing Ltd British Journal of Haematology 149, 35-49 <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2009.08054.x/epdf>

## Appendix 3 – Sick Cell Disease

Genotype	Anaemia	Splenomegaly	Clinical features	Clinical severity	Remarks/treatment
Sickle Cell Anaemia  (Hb SS)	Severe	Yes  Usually auto-splenectomy  by age 5-7 years	Vaso-occlusive episodes (painful crisis)  Bone and joint infarcts  Hepato-renal complications  Bacterial infections  If Hb F is elevated then condition may be milder than usual	Severe	Progressive disability common. Usually shortened life span. Bone marrow transplant may be considered (in children) if there is severe disease and an HLA matched sibling is available.  <b>Treatment:</b> Oral Penicillin is routinely prescribed for children but is optional for adults  Pneumococcal vaccine (adults & children)  Folic acid depending on diet and/or local protocol
Haemoglobin SC Disorder  (Hb SC)	Mild to moderate  Hb level is just below normal	Common	Intermittent painful crises  Bone and joint infarcts (less common than in SS)  Retinopathy in adults  May have aseptic necrosis of joints	Variable	Severity often increased during pregnancy  May present with any of the same symptoms as Sickle Cell Anaemia but condition is usually milder.  <b>Treatment:</b> Oral Penicillin is <i>routinely prescribed</i> for children but <i>is optional</i> for adults  Pneumococcal vaccine (adults & children)  Folic acid depending on diet and/or local protocol

Genotype	Anaemia	Splenomegaly	Clinical features	Clinical severity	Remarks/treatment
<p>S/β thalassaemia</p> <p>This is inclusive of</p> <p>Hb S/β<sup>+</sup>, Hb S/δβ,</p> <p>Hb S/γδβ and</p> <p>Hb S/Lepore</p>	Mild to moderate	Occasional	<p>Intermittent pain crises</p> <p>Bone and joint infarcts</p>	<b>Variable</b>	<p><b>Treatment:</b> Oral Penicillin is <i>routinely prescribed</i> for children but <i>is optional for adults</i></p> <p>Pneumococcal vaccine (<i>adults &amp; children</i>)</p> <p>Folic acid depending on diet and/or local protocol</p>



Genotype	Anaemia	Splenomegaly	Clinical features	Clinical severity	Remarks/treatment
S/ $\beta^0$ Thalassaemia	Moderate to severe	Common	Intermittent pain crises  Bone and joint infarcts  Severity depends on type of beta ( $\beta$ ) thalassaemia gene inherited and % of Hb F produced	<b>Moderate to severe</b>	May be as severe as Sickle Cell Anaemia, depends on the thalassaemia mutation inherited. No normal Hb A.  Treatment: Oral Penicillin is <i>routinely prescribed</i> for children but <i>is optional for adults</i>  Pneumococcal vaccine (adults & children),  Folic acid depending on diet and/or local protocol
Haemoglobin S/D <sup>Punjab</sup>  Disorder  (HbSD <sup>Punjab</sup> )	Mild to moderate haemolytic anaemia	Common	Severity of clinical picture is variable but usually milder than sickle cell anaemia	<b>Variable</b>	Treatment: Oral Penicillin is <i>routinely prescribed</i> for children but <i>is optional for adults</i>  Pneumococcal vaccine (adults & children),  Folic acid depending on diet and/or local protocol
Haemoglobin S/O <sup>Arab</sup>  Disorder  (HbSO <sup>Arab</sup> )	Mild to moderate haemolytic anaemia		Usually mild to moderate condition	<b>Variable</b>	Treatment: Oral Penicillin is <i>routinely prescribed</i> for children but <i>is optional for adults</i>  Pneumococcal vaccine (adults & children),  Folic acid depending on diet and/or local protocol

Genotype	Anaemia	Splenomegaly	Clinical features	Clinical severity	Remarks/treatment
Haemoglobin S/E Disorder  (Hb SE)	May have normal haemoglobin levels		Usually asymptomatic or very mild	Variable	Treatment: Oral Penicillin is <i>routinely prescribed</i> for children but <i>is optional</i> for adults  Pneumococcal vaccine (adults & children),  Folic acid depending on diet and/or local protocol
Haemoglobin S/HPFH	Mild haemolytic anaemia  but haemoglobin level is usually normal		Usually asymptomatic or very mild		<b>Not distinguishable on newborn screening from</b>  S/ $\beta^0$ thalassaemia or Sickle Cell Anaemia (Hb SS) on initial newborn screen  <b>Usually no regular treatment required</b> once diagnosis is confirmed  Regularity of monitoring by Specialist varies dependent on local protocol

Notes

**It is not possible at birth to differentiate with certainty between sickle cell anaemia (HbSS), Hb S/ $\beta^0$  thalassaemia and Hb S with hereditary persistence of fetal haemoglobin (Hb S/HPFH), since all of these conditions produce only Hb F and HbS on routine analysis.**

- Offer genetic counselling and prenatal diagnosis to women/couples at risk of having a baby with any of the above conditions (except S/HPFH)

- Individuals with these conditions should be registered with and followed up regularly by a Haematology Clinic
- Pregnant women with any of the above sickle cell disorders should be considered as being “high risk” and should be followed up by a Haematologist and Obstetrician during pregnancy with booked hospital delivery.

## References

Bain BJ (2006) *Sickle cell haemoglobin and its interactions with other various haemoglobins and with thalassaemia*. Haemoglobinopathy Diagnosis, 2<sup>nd</sup> Edition Blackwall Publishing Ltd

Brent Sickle Cell & Thalassaemia Centre (2012) *A Parent's Guide to Managing Sickle Cell Disease* <https://www.gov.uk/government/publications/sickle-cell-disease-managing-the-condition>

NHS Sickle Cell & Thalassaemia Screening Programme (2012) *Handbook for Laboratories*. 4<sup>th</sup> Edition.  
<https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-handbook-for-laboratories>

Thalassaemia International Federation (TIF) *About Sickle Cell Disorders*. <http://www.thalassaemia.org.cy/>

## Appendix 4 – Thalassaemia Conditions

Genotype	Anaemia	Splenomegaly	Other clinical features	Clinical severity	Remarks/treatment
Beta ( $\beta$ ) <b>Thalassaemia Major</b> <b>(<math>\beta</math>thal/<math>\beta</math>thal)</b>	Severe  Impaired red blood cell production	Common  May require splenectomy	Endocrine dysfunction Cardiac failure Iron overload Hepatic dysfunction Increased risk of infections	Severe  Shortened life span if untreated or inadequately treated	Decreased synthesis of $\beta$ globin chains. Presents in infancy. <b>Treatment:</b> Blood transfusions and iron chelation therapy for life. Bone marrow transplant if HLA matched donor. <b>Offer counselling and PND to couples 'at risk' of having a baby with this condition.</b>
E/ $\beta$ Thalassaemia  (Hb E/ $\beta$ thal)	Moderate to severe	Common	Iron overload  Cardiac failure  Hepatic dysfunction  Endocrine dysfunction  Cholelithiasis  Increased risk of $\uparrow$ infections	Very variable may range from mild to severe	<b>May present as severe as <math>\beta</math> Thalassaemia Major (requiring blood transfusions and iron chelation for life) or as <math>\beta</math> Thalassaemia Intermedia.</b>  <b>Folic acid supplements needed.</b>  Bone marrow transplant may be indicated depending on severity of condition.  <b>Offer counselling and PND to couples 'at risk' of having a baby with this condition.</b>
Thalassaemia Intermedia  <b>(could be caused by a range of haemoglobinopathies – see carrier chart)</b>	Mild to moderate	Common	Usually moderate to mild thalassaemic condition depending on genetic mutations inherited	Moderate  Possible iron overload	DNA needed to confirm genotype/severity  <b>Usually no regular treatment required but may need occasional blood transfusions for example during pregnancy or infection</b>

for further information)			Usually presents after 2 years of age if not identified at birth  Osteoporosis  Renal calculi		<b>Folic acid supplements may be beneficial.</b>  <b>Regular monitoring by Specialist even if no treatment is required.</b>  <b>Assessment by specialist if a couple are at risk of having a baby with this condition.</b>
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Genotype	Anaemia	Splenomegaly	Other clinical features	Clinical severity	Remarks/treatment
Hb "H Disease" <b>(Alpha Thalassaemia 3 gene deletion --/-α)</b>	Mild to moderate	Occasional	Occasional haemolytic anaemia  Gallstones	Mild to moderate	<b>No regular treatment required</b> but haemoglobin levels may fall during infection or episode of anaemia so occasional blood transfusion may be needed. Regular monitoring by Specialist is important.  <b>Genetic counselling but PND not indicated</b>
Alpha (--/--) Thalassaemia Major	Severe intrauterine anaemia	Not applicable	Also known as Haemoglobin Barts Hydrops Fetalis  Associated with maternal morbidity & mortality if undetected during	Very severe  Absence of all 4 alpha (α) globin genes	Incompatible with life in utero as no fetal haemoglobin is produced.  The use of intra uterine blood transfusion has been used on occasion. Most common in Far East Asia.

			pregnancy		Offer counselling and PND to couples 'at risk' of having a baby with this condition.
--	--	--	-----------	--	--

#### Notes

- Individuals with these conditions (except alpha thalassaemia major) should be registered with and followed up regularly by a Haematology Clinic
- Pregnant women with any of the above disorders should be considered “*high risk*” and should be followed up by a Haematologist and Obstetrician during pregnancy with booked hospital delivery.

#### References

Eleftheriou A, Angastiniotis M [About Alpha Thalassaemia](#) Thalassaemia International Federation (TIF) [www.thalassaemia.org.cy](http://www.thalassaemia.org.cy)

Eleftheriou A, Angastiniotis M [About Beta Thalassaemia](#) Thalassaemia International Federation (TIF) [www.thalassaemia.org.cy](http://www.thalassaemia.org.cy)

NHS Sickle Cell & Thalassaemia Screening Programme (2017) *Handbook for Laboratories. 4<sup>th</sup> Edition*.  
<https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-handbook-for-laboratories>

Ryan et al on behalf of the British Committee for Standards in Haematology (2010) *Significant haemoglobinopathies: guidelines for screening and diagnosis*. Blackwall Publishing Ltd British Journal of Haematology 149, 35-49 <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2009.08054.x/epdf>

## Appendix 5: DNA Laboratory contact details

### John Radcliffe Hospital Oxford

Contact Dr Melanie Proven, Principle Clinical Scientist  
e-mail [hbopathy.screening@nhs.net](mailto:hbopathy.screening@nhs.net) or [molhaem@ouh.nhs.uk](mailto:molhaem@ouh.nhs.uk)  
[oxford.molecularhaem@nhs.net](mailto:oxford.molecularhaem@nhs.net)  
Tel 01865572769/ 01865572826  
Fax 01865572775  
Address: Molecular Haematology  
Level 4  
John Radcliffe Hospital  
Headington, Oxford, OX39DU  
Web site: <http://www.oxford-translational-molecular-diagnostics.org.uk/>  
Link for PND referral form: <http://www.oxford-translational-molecular-diagnostics.org.uk/content/forms>

### King's College Hospital

Contact Dr Barnaby Clark, Principal Clinical Scientist  
e-mail [barnaby.clark@nhs.net](mailto:barnaby.clark@nhs.net)  
Tel 020 32994337  
Tel lab 020 3299 9000 Ext 2265  
Fax 020 32991035  
Lab Email [kch-tr.PND@nhs.net](mailto:kch-tr.PND@nhs.net)  
Address: C /O Central Specimen Reception  
Blood Sciences Laboratories  
Ground Floor Bessemer Wing  
King's College Hospital  
Denmark Hill  
London SE5 9RS  
Link for PND referral form: <http://www.viapath.co.uk/our-tests/prenatal-diagnosis>

### University College London Hospital

Contact Dr Mary Petrou, Director Haemoglobinopathy Genetics Centre  
e-mail [mary.petrou@uclh.nhs.uk](mailto:mary.petrou@uclh.nhs.uk)  
Tel 020 34479458  
Fax 02034479864  
E-mail [haemoglobinopathygenetics@nhs.net](mailto:haemoglobinopathygenetics@nhs.net)  
Address: Haemoglobinopathy Genetics Centre  
Molecular Genetics Laboratory  
307 Euston Road  
London NW1 3AD  
Link for PND referral form: <https://www.uclh.nhs.uk/OurServices/ServiceA-Z/PATH/PATHHT/PATHHAEMGEN/Pages/Home.aspx>

### Central Manchester University Hospitals NHS Foundation Trust

Contact Steve Keeney, PhD Lead Clinical Scientist, Molecular Haematology Service  
e-mail [steve.keeney@cmft.nhs.uk](mailto:steve.keeney@cmft.nhs.uk)  
Tel 0161 276 5990 / 4809  
Fax 0161 276 5989  
Website <http://www.cmft.nhs.uk/haemoglobinopathy>  
Address: Molecular Diagnostics Centre  
The Manchester Centre for Genomic Medicine  
6th Floor, St Mary's Hospital  
Oxford Road  
Manchester, M13 9WL  
Link for PND referral form: <http://www.cmft.nhs.uk/info-for-health-professionals/laboratorymedicine/haematology/haemoglobinopathy>

## Appendix 6 - Antenatal Counselling Form

Brent Sickle Cell & Thalassaemia Centre (NW London Hospitals NHS Trust)			
Antenatal Screening and Counselling Form			
Client		Partner	
Surname		Surname	
First name		First name	
Address		Address	
Tel		Tel	
DoB		DoB	
NHS No.		NHS No.	
Hospital No.		Hospital No.	
GP		GP	
Address/Tel.		Address	
Ethnic Group		Ethnic Group	
Language spoken		Language spoken	
Interpreter needed	Yes <input type="checkbox"/> No <input type="checkbox"/>	Interpreter needed	Yes <input type="checkbox"/> No <input type="checkbox"/>
Occupation		Occupation	
Religion		Religion	

### Haematology Results

	Date Tested	Hb Type	Hb	RBC	MCV	MCH	A <sub>2</sub>	F	Result to patient	Result to patient for GP
Client										
Partner										

At risk Couple? Yes ☐ No ☐ Couple informed of risk? Yes ☐ No ☐  
 GP informed of risk? Yes ☐ No ☐ ANC informed of risk? Yes ☐ No ☐

Obstetric History	Hospital	Consultant
LMP	Gest. Age at testing	EDD

Client prev. counselled	Yes <input type="checkbox"/> No <input type="checkbox"/>	Hosp. where tested	Where Counselling	Hb Result
Partner prev. tested	Yes <input type="checkbox"/> No <input type="checkbox"/>	Hosp. where tested	Date tested	Hb Result

### Details of Children

Name	DoB	Hospital	M/F	Hb Type	Comments



## Counselling Details

Date of appointments: [1] ...../...../.....[2] ...../...../..... Gest. age at counselling: ...../40

Attended with partner ☐ Attended alone ☐ Partner attended alone ☐ Did not attend ☐

Partner Screening: Blood sample taken ☐ Laboratory forms given / Sent ☐ date

sent.....

Reason for not attending (if known): .....

### Information discussed

	Yes	No	N/A
1. Difference between blood group and Hb type	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. What is a red blood cell and its function	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Types of haemoglobin (normal and abnormal)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Population affected and proportion	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Clinical effect of trait/disease	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Genetic and health implications for nuclear and extended family	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Testing offered to other family members	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Client understanding checked	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

### Prenatal Diagnosis

Discussed?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Offered?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Accepted?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

If PND not accepted, reason given: .....

If PND accepted, name of Dr: ..... Centre referred to: ..... Result of PND: .....

At risk- couple letter to parents to inform Centre of birth: Yes ☐ No ☐ If no state reason: .....

Termination of pregnancy? Yes ☐ No ☐

### Post ToP contact

Outcome of contact: .....

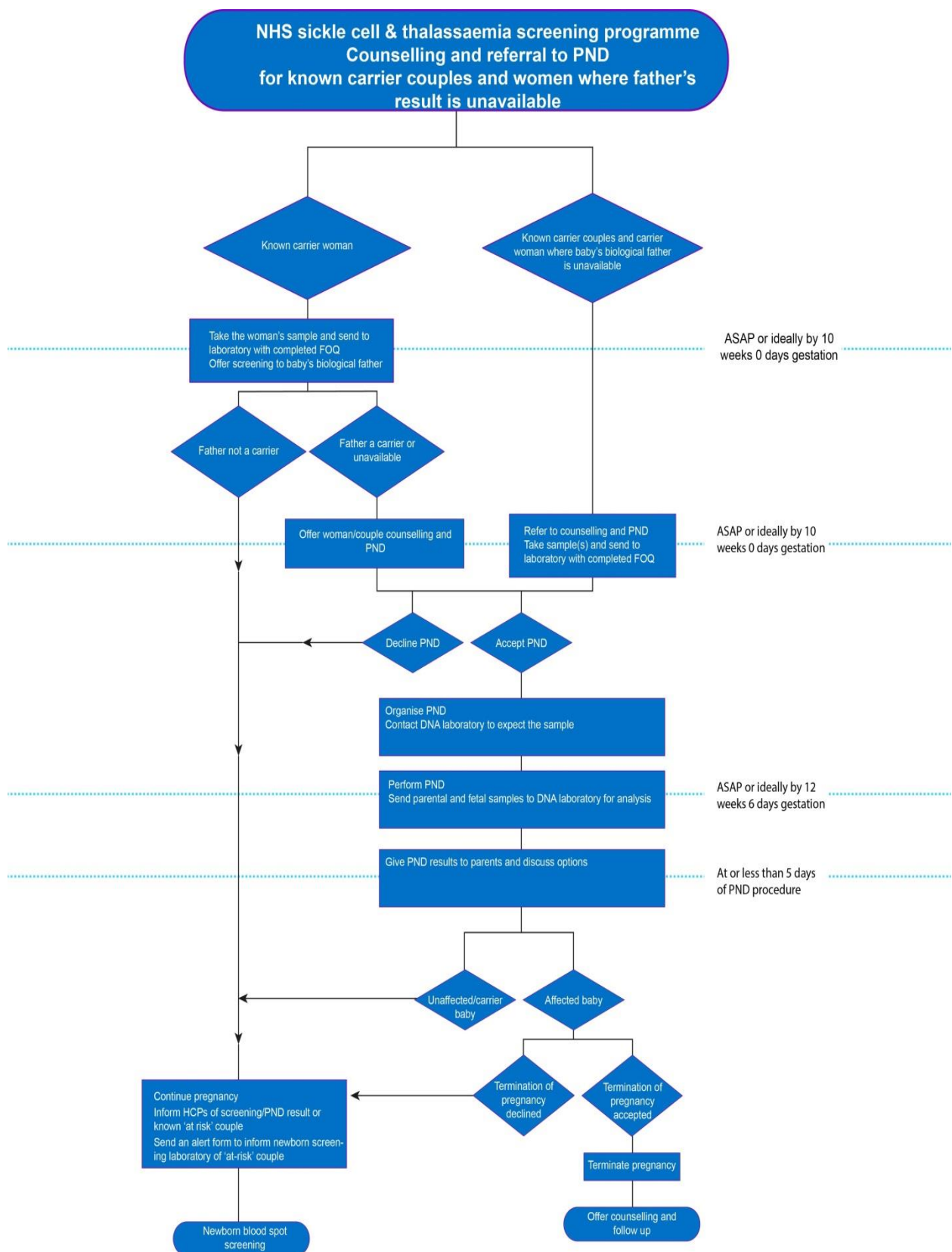
### Neonatal Outcome

Registered Name: ..... DoB: ...../...../..... Sex: M ☐ F ☐ Lab No: .....

NHS No: ..... Neonate Result Hb type: ..... Date Parents informed of baby's result: .....

PND Centre informed of Neonatal result (if relevant): Yes ☐ No ☐

## Appendix 7: “At risk couples” flow chart



## Appendix 8: At risk pregnancy alert form

### AT RISK PREGNANCY ALERT FORM

Maternal Surname	First Name	Date of Birth	NHS Number	Hb'opathy screen result	Place of test	Date of test
Paternal Surname	First Name	Date of Birth	NHS Number	Hb'opathy screen result	Place of test	Date of test
Maternal Address Including Postcode				Telephone Number (Home)		Mobile Number
GP Address Including Postcode				GP Name		GP Telephone Number
Gravida/Parity	EDD	Gestation	Maternity Unit Name & Address			Named Obstetrician
Referrer's Name	Referrer's Telephone #	Date of referral	Had PND this pregnancy?	PND Result	Referrer's Signature	Date of referral
			Yes: <input type="checkbox"/> No: <input type="checkbox"/>			
Comments/Other relevant information/Relevant Family History						
<b>Report Back To Referrer</b>						
Baby's Surname	Baby's First Name	Male/Female	Baby's DOB	Baby's NHS Number	Baby's Address	
Date of Specimen	Date of Test	Baby's Newborn Screening Result			Signature	Date
Comments/Other Relevant Information						

Please send completed form for all "at risk" couples who continue the pregnancy, (whether or not they have had prenatal diagnosis) to

- newborn screening laboratory
- counselling service/team who follow up newborn screening results

## Appendix 9: NHS Sickle Cell and Thalassaemia Screening Programme prenatal diagnosis (PND) outcome form

Dear requesting clinician,

The National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) collect screening results and outcomes for the NHS SCT screening programme on pregnant women who have opted for PND; data is collected from the PND laboratories.

NCARDRS has permission from the National Information Governance Board under section 251 the NHS Health ACT 2006 and the authority of the Health Service (Control of Patient Information) Regulations 2002, to collect patient-identifiable data without the need for individual informed consent (CAG ref: CAG 10-02(d)/2015).

The main aim is evaluate the screening programme. **To achieve this, please send this outcome form to the screening co-ordinator or specialist nurse at the maternity unit providing antenatal care.** Women can opt out of the register at any time, for more information see [www.gov.uk/phe/ncardrs](http://www.gov.uk/phe/ncardrs).

For more information on this work please contact the PND laboratory or email the PHE Screening helpdesk at [phe.screeninghelpdesk@nhs.net](mailto:phe.screeninghelpdesk@nhs.net). Thank you very much for your help with this important work.

### PND outcome form **Part 1** – short-term pregnancy outcome

<b>Part A</b> - please forward to requesting unit		<b>Outcome form unique number</b>		
<b>Maternal surname</b>	<b>First name</b>	<b>DoB</b>	<b>NHS Number</b>	<b>EDD</b>
<b>Maternal address</b>		<b>GP name and address</b>		<b>PND reference</b>

..... cut here .....

## PND outcome form **Part 1** – short-term pregnancy outcome

<b>Part B</b> To be completed by the screening coordinator or specialist nurse and returned to PND lab within one month of receiving PND result		Outcome form unique number:	
Maternity unit address	Date of referral	Referrer's name	PND result
<b>Please tick outcome:</b> CONTINUING PREGNANCY [ ] MISCARRIAGE [ ]* TERMINATION OF PREGNANCY [ ]*			
*If there is a miscarriage or termination of pregnancy, do not complete Part 2 of the outcome form			
<b>Completed by</b> (please print)  NAME  TELEPHONE		<b>Date</b> Part 1 B completed on	

## PND outcome form **Part 2** – final outcome

<b>Part A</b> – please forward to requesting unit		Outcome form unique number		
Maternal surname	First name	DoB	NHS Number	EDD
Maternal address		GP name and address		PND reference
Maternity unit address		Date of referral	Referrer's name	PND result

..... cut here .....

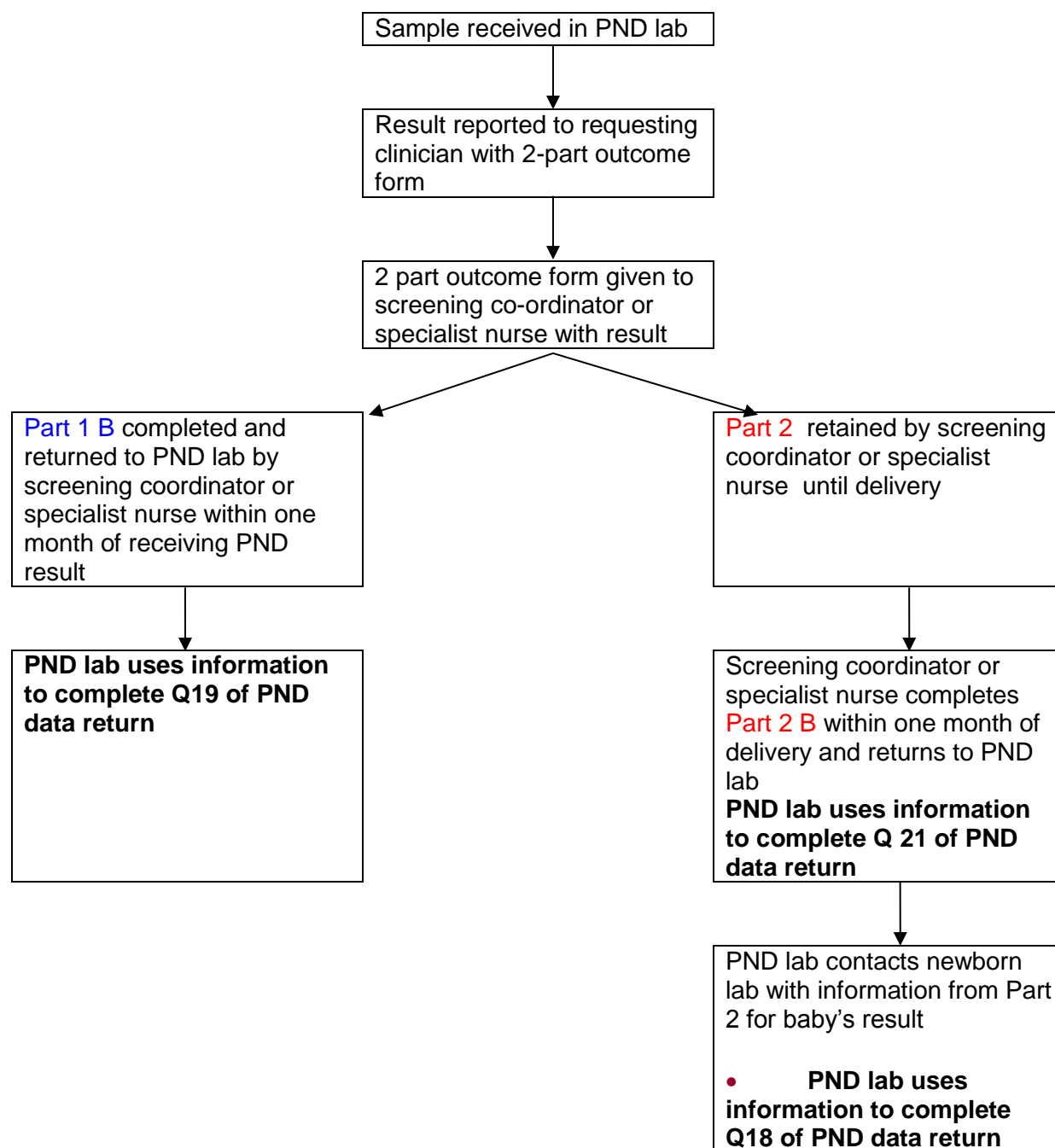
## PND outcome form **Part 2** – final outcome

<b>Part B</b> to be completed within one month of delivery by screening coordinator or specialist nurse and returned to PND lab		<b>Outcome form unique number:</b>	
<b>Maternity unit address</b>	<b>Date of referral</b>	<b>Referrer's name</b>	<b>EDD</b>
<b>Please return to</b> PND lab address		<b>Please return by</b> (one month from EDD)	
<b>Baby's NHS Number</b>	<b>Newborn laboratory that baby's blood spot was sent to</b>	<b>Baby's place of birth</b>	<b>If no live birth, please give reason</b>
<b>Completed by</b> (please print)  Name:  Telephone:		<b>Date</b> Part 2 B completed on	

Please complete parts in **red**, retain the named portion of this form (Part 2 A), and only return **Part 2 B** Final Outcome Form, with its unique identifying number to the PND laboratory

Version 20 June 2017

### Flow diagram for use of 2-part pregnancy outcome form



The form should be sent for all PND requests, not just those where PND shows an affected fetus.

The screening co-ordinator or specialist nurse is only required to complete parts in red and blue.

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## Appendix 10 Follow up of newborn DNA screening results

### DNA for Transfused Babies

#### Counselling Notes for Health Care Professionals

Babies who have had a blood transfusion prior to newborn screening for sickle cell disease do not have a reliable screening result. The NHS Sickle Cell & Thalassaemia Screening Programme supports testing these samples using a DNA process. Although it is not the same quality as the routine screening processes, babies with sickle cell disease who may be missed for timely follow up and care should be identified via the test.

#### No sickle cell gene (mutation) detected

##### Counselling Notes

A negative result means that the individual does not carry the sickle cell gene mutation on any chromosome. The baby does not have sickle cell disease but this does not exclude other haemoglobin variants or conditions such as

- Hb C, Hb O<sup>Arab</sup>, Hb D<sup>Punjab</sup>, Hb E, Hb Lepore or any unstable Hb variant (carrier states)
- Beta thalassaemia major
- Beta thalassaemia carrier
- $\delta\beta$  thalassaemia;  $\gamma\delta\beta$  thalassaemia;  $\epsilon\gamma\delta\beta$  thalassaemia
- Hereditary Persistence of Fetal Haemoglobin (HPFH)
- Alpha thalassaemia
- Benign haemoglobin disorders (for example Hb CC; C/Beta thalassaemia; DD; EE etc)

**Review** parental haemoglobinopathy results and advise accordingly. **It is NOT the responsibility of the health care professional to initiate the repeat blood test**, but parents should be assisted with this process if required. The sample should be liquid blood and sent to the specialist haematology laboratory linked to the Clinical Network, at least 4 months after the last blood transfusion was given.

#### Sickle cell gene (mutation) plus another haemoglobin gene

##### Counselling Notes

This individual is most likely to be a sickle cell carrier but a compound heterozygous condition with another haemoglobin variant or a beta thalassaemia mutation cannot be excluded. The possible outcomes are listed below.

**A carrier of Hb S (Hb AS genotype)**

**OR Sickle cell disease**

- HbSC
- HbS/O<sup>Arab</sup>
- HbS/D<sup>Punjab</sup>
- HbS/Lepore
- HbS/ $\beta^0$  thalassaemia
- HbS/ $\beta^+$  thalassaemia
- S/HPFH

**Please follow up via the appropriate clinical pathway for possible sickle cell disease patients** for confirmation of diagnosis and counselling. Parental haemoglobinopathy results should be checked where possible.

#### Only the sickle cell gene (mutation) detected

##### Counselling Notes

**Please follow up via the appropriate clinical pathway for newly diagnosed children with sickle cell disease.** This individual is likely to be affected by sickle cell disease. Review parental haemoglobinopathy results. Babies should commence penicillin prophylaxis routinely while diagnosis is being confirmed.

**If you have any queries please contact the NHS Sickle Cell and Thalassaemia Screening Programme** Email: [PHE.screeninghelpdesk@nhs.net](mailto:PHE.screeninghelpdesk@nhs.net)



## Appendix 11 Affected baby counselling form

### Brent Sickle Cell & Thalassaemia Centre (NW London Hospitals NHS Trust) Neonatal Screening and Counselling Form

#### DETAILS OF BABY

Birth Surname ..... District .....

Registered Surname ..... Hospital of Birth .....

First Name ..... D.o.B ...../...../..... Sex M ☐ F ☐

Address ..... Hb Genotype (*final result*).....

..... Lab No. .... NHS No. ....

..... Date card & leaflet sent ...../...../.....

Tel. No. .... Transfused YES ☐ NO ☐

..... If YES enter date of last transfusion ...../...../.....

**Affected Baby:** Hospital referred..... Name Paediatrician.....

Notification to GP/ HV /Parents..... Date of 1<sup>st</sup> Hospital Appt.....

Date 1<sup>st</sup> prescribed Penicillin:..... Date 1<sup>st</sup> Primary Vac:.....

HV Details:.....

#### DETAILS OF PARENTS (Enter surname first in CAPITAL letters, then first name)

Mother ..... Father .....

DoB ...../...../..... NHS No:..... DoB ...../...../..... NHS No:.....

Ethnic Origin ..... Ethnic Origin .....

Religion ..... Religion .....

GP ..... GP .....

Need Interpreter YES ☐ NO ☐ Language .....

#### HAEMATOLOGY RESULTS (Parents)

PND YES ☐ NO ☐ Outcome:.....

	Date Tested	Hb Type	Hb	RBC	MCV	MCHC	A <sub>2</sub>	F	Sickle Test	Lab confirmed Yes/No	Screened At
Mother											
Father											

Date(s) card(s) sent: Mother ...../...../..... Father...../...../..... GP notified ...../...../.....

#### DETAILS OF SIBLINGS

Name	DoB	Place of Birth	Sex	Date Tested	Hb Type	Comments