

Testing for and Diagnosis of Sickle Cell Disease and Thalassaemia in Children

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Guidelines on Testing for and Diagnosis of Sickle Cell Disease and Thalassaemia in Children

Abstract Page

This guideline is aimed at staff dealing with all children seen in King's College Hospital who might have sickle cell disease or thalassaemia. It should be of use to paediatric and haematology doctors and nurses, but may also be useful to any member of the multidisciplinary team.

Haemoglobinopathy Screening in England

All babies born in England are screened for sickle cell disease (SCD) and thalassaemia major, by heel prick testing in the first few days of life. Therefore, all babies born in England with SCD or thalassaemia should have already been diagnosed and the parents informed of the likely diagnosis usually by the community sickle cell nurse specialists. They are then referred to the paediatric haematology clinic for further counselling and confirmatory testing which should occur by 3 months of age. Babies born locally will have been tested in the Neonatal Screening Laboratory at St Thomas' Hospital and confirmed in the King's laboratory if abnormal. Results are available by telephoning extension 7632.

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Guidelines on Testing for and Diagnosis of Sickle Cell Disease and Thalassaemia in Children

Definition/Background

This guideline is aimed at staff dealing with all children seen in King's College Hospital who might have sickle cell disease or thalassaemia. It should be of use to paediatric and haematology doctors and nurses, but may also be useful to any member of the multidisciplinary team.

Haemoglobinopathy Screening in England

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However, the diagnosis of SCD or Thalassaemia Major should also be considered in other situations as outlined below.

Pre – Requisites for Practitioner

An understanding of the indications for testing; no particular expertise is required but please discuss any concerns with the paediatric haematology team as suggested below.

Indications: Which children should be tested?

(a) Sickle Cell Disease:

- **Ethnic origin should not be used to decide who should be tested**, due to the large numbers of people with mixed family origins and the difficulty of determining ethnic origin accurately. Diagnostic testing should be sent on all children born outside the England, unless there is clear documentation of the presence or absence of SCD, which may be in the hospital notes, EPR or possibly in hand-help patient records or letters. If there is any doubt, testing should be requested. If the child was born in England it should be possible to find the results of neonatal screening, although repeat testing may be necessary if there is doubt. Older children in particular, may have been born before universal neonatal screening was introduced.
- **Acute illness**: the diagnosis should be considered in all children presenting with unexplained acute illness, including acute pain, anaemia, acute neurological symptoms, loss of vision, collapse, respiratory symptoms, hepatosplenomegaly, jaundice, swollen limbs and sepsis.
- **To confirm the diagnosis of SCD**: Children are referred to the paediatric haematology clinic following the diagnosis of SCD on neonatal screening. The diagnosis should be confirmed by repeat testing to exclude diagnostic errors, sample mislabelling etc.
- **Preoperatively**: the sickle status of children should be known prior to anaesthetic. This might be available because of prior testing or screening, if not, specific testing should be requested and the results known before proceeding.
- **Opportunistic testing**: siblings of children with SCD should be offered testing unless their haemoglobinopathy status is known. Similarly it may be appropriate to offer testing to parents and other relatives.

(b) Severe Thalassaemia:

- Severe thalassaemia is typically due to the inheritance of β thalassaemia alleles from both parents.
- **The diagnosis should be considered** in any child with unexplained anaemia, particularly if there is also microcytosis, failure to thrive, splenomegaly, bony expansion or extramedullary haematopoiesis. Many, but not all, cases born in England are detected by neonatal screening.
- **To confirm the diagnosis of severe thalassaemia**; children are referred to the paediatric haematology clinic following the diagnosis on neonatal testing. The diagnosis should be confirmed on repeat testing to exclude diagnostic errors, sample mislabelling etc
- **Opportunistic testing** of relatives of affected children may be appropriate as for SCD.

Equipment required

EDTA (FBC) blood bottles – see below

Salivary DNA kit – see below

Guideline steps – What tests should be requested?

(a) Sickle Cell Disease:

Tests are performed on blood taken into EDTA tubes. The results of all tests can be misleading if a blood transfusion has been given in the last four months due to the presence of transfused HbA, and children with sickle cell disease may appear to be carriers. Tests should therefore be requested before any blood transfusion, or if this is not possible, the timing of any transfusion should be included on the request form, to assist interpretation of the result.

Urgent testing: in acutely unwell children, 'Sickle cell & thalassaemia screen' should be requested urgently on EPR and also discussed with the laboratory. Out-of-hours testing may involve a sickle solubility test, which does not distinguish between carriers and those with SCD, so it is safest to assume SCD is present until definitive results are available. However, in general, if the haemoglobin is $>12\text{g/dl}$ the child is unlikely to have SCD.

Confirmatory testing: 'Sickle cell & thalassaemia screen' should be requested on EPR. In infants seen for confirmatory testing, a salivary DNA sample can be taken to avoid the need for blood testing; this is currently not available on EPR and should be discussed with Professor Rees, Dr Height or Dr Dick first. The sample needs to be taken using a specific mouth-swab kit, and given personally to Dr Barnaby Clark in the prenatal diagnosis laboratory (Ext 3242). The type of sickle cell disease may be unclear, particularly if both parents are not available for testing and DNA analysis may be helpful in these circumstances, and should be discussed with one of the paediatric haematology consultants; this is requested as 'Haemoglobin DNA investigation' on EPR.

Preoperative testing: this is requested on EPR as 'sickle cell screen (preop) (preanaesthetic sickle cell screen) and an EDTA blood sample sent.

Tests Used to Monitor Children with Sickle Cell Disease on Treatment

1. **Haemoglobin S quantitation (HbS%):** this is useful in children receiving regular blood transfusions, or when a transfusion has been given for an acute complication, such as acute chest syndrome or stroke. Depending on the problem, the aim typically will be to achieve a target HbS% of less than 30% or 50%. It is not useful to measure HbS% in children not receiving blood transfusions, and variations in HbS% do not help to diagnose the cause or severity of complications.
2. **Haemoglobin F quantitation (HbF%):** this is most often used to monitor the effect of hydroxyurea (hydroxycarbamide). It is also performed at intervals throughout childhood as part of annual review of children with SCD; a lower HbF% is associated with a more severe

clinical course, however, it is not useful to assess the cause or severity of acute complications.

(b) Severe Thalassaemia:

'Sickle cell & thalassaemia' screen should be requested, ideally before any blood transfusion is given. DNA analysis is typically needed to confirm the diagnosis, but this will usually be arranged in the paediatric haematology clinic.

Follow-up After Testing

Typically results are available after 2-3 days. Arrangements should be made with the carers to ensure that they and the child receive the results. This may involve telephoning the results although written confirmation should always be sent. If a child is found to have SCD or severe thalassaemia, this should be discussed with a member of the paediatric haematology team. The parents should be informed of the result, and a written referral made urgently to the paediatric haematology clinic. The child will usually be seen within 2 weeks. If the child has SCD, it may be appropriate to start antibiotic prophylaxis immediately.

Other information

Related guidelines & parent/patient information

A parent's guide to managing sickle cell disease – given to parents of all newly diagnosed children with SCD. Further copies can be obtained from the SE London Sickle Cell & Thalassaemia Centre 0203 049 5993

References

K Ryan, BJ Bain, D Worthington, J James, D Plews, A Mason, D Roper, DC Rees, B de la Salle and A Streetly on behalf of the British Committee for Standards in Haematology. Significant haemoglobinopathies: guidelines for screening and diagnosis. British Journal of Haematology 2010, doi:10.1111/j.1365-2141.2009.08054.x.