King's College Hospital NHS
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Guidelines on 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

This guideline is aimed at 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 should be screened for sickle cell disease (SCD) in the first few days of life by neonatal heelprick testing. Therefore all babies born in England with SCD should have already been diagnosed and the parents informed of the diagnosis. Babies born locally will have been tested in the Neonatal Screening Laboratory at King's College Hospital and results may be available by telephoning extension 7632.

Sickle Cell Disease

Which children should be tested?

1. Acutely ill children: the diagnosis should be considered in all children presenting with unexplained acute illness, including acute pain in any part of the body, anaemia, acute neurological symptoms, loss of vision, collapse, respiratory symptoms, hepatosplenomegaly, jaundice, swollen limbs and sepsis. 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 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.
2. 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.
3. Preoperatively: the sickle status of children should be known prior to anaesthetic. This might often be available because of prior testing or screening, although specific testing should be requested if the results are not available.
4. 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.

What tests should be requested?

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, and in particular, 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.

1. Urgent testing: in acutely unwell children, 'Sickle cell and thalassaemia screen' should be requested urgently. Urgent requests should be discussed with the laboratory. Out-of-hours testing may involve a sickle solubility test, which does not distinguish between carriers and those with SCD, although it is safest to assume SCD is present until definitive results are available. In general, if the haemoglobin is >12g/dl the child is unlikely to have SCD.
2. Confirmatory testing: 'Sickle cell and thalassaemia screen' should be requested on EPR. In infants seen for confirmatory testing, a mouth-swab DNA sample can be taken to avoid the need for blood testing; this is currently not available on EPR and should be discussed with Dr 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. The type of sickle cell disease may be unclear, particularly if both parents are not available for testing. 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.
3. Preoperative testing: this is requested as 'sickle cell screen (preop)(preanaesthetic sickle cell screen).

Tests Used to Monitor Children with Sickle Cell Disease on Treatment

1. Haemoglobin S quantitation: 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. Typically the aim will be to achieve a target haemoglobin S percentage of less than 30% or 50% depending on the problem. It is not useful to measure Haemoglobin S percentage in children not receiving blood transfusions, and variations in HbS levels do not help to diagnose the cause or severity of complications.
2. Haemoglobin F quantitation: this is most often used to monitor the effect of hydroxyurea. It is also performed at regular intervals throughout childhood as part of annual review, as lower haemoglobin F levels are associated with a more severe clinical course. As for haemoglobin S quantitation, it is not useful to assess the cause or severity of acute complications.

Severe Thalassaemia

Which children should be tested?

1. Severe thalassaemia is typically due to the inheritance 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
2. Opportunistic testing of relatives of affected children may be appropriate as for SCD.

What tests should be requested?

‘Sickle cell and 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 a 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.

Reference

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. Br J Haematol. 2010, doi:10.1111/j.1365-2141.2009.08054.x.

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