

# NHS Sickle Cell & Thalassaemia Screening Programme

## DNA for Transfused Babies

### Guidance for Implementation & Follow Up

#### Background

Newborn screening for sickle cell disease was fully implemented throughout England in 2006. Data received from the 13 newborn screening laboratories in England show 666,060 babies were screened in 2007/08 via the bloodspot card. Of these, 359 were identified with significant sickle cell conditions requiring follow up and treatment. During the same time period 9,452 babies were identified as carriers of haemoglobin variants and 3,725 babies received a blood transfusion prior to screening.<sup>1</sup>

The outstanding area of grave concern in newborn screening for sickle cell relates to the possibility of babies being undiagnosed as having sickle cell disease, due to having a blood transfusion prior to a bloodspot sample being taken. These babies do not have a valid sickle cell screen result. Currently, the Guidelines for Newborn Bloodspot Testing recommend taking one bloodspot prior to transfusion.<sup>2</sup> Alternatively, if this is not carried out, the recommendation is for repeat testing at 4 months post last blood transfusion using a liquid sample of blood. However this is challenging as it is a difficult, costly and very time consuming process for primary care and specialist counselling staff to administer. For babies that have multiple transfusions, the repeat testing policy could result in a considerable delay in being tested for sickle cell disease with the potential risk of missing a baby with the condition.

The difficulties with the repeat testing process are well highlighted by audit data from Sheffield Children's Hospital which showed that only 3 babies out of 24 were retested in a timely manner following transfusion.<sup>3</sup> At King's College Hospital,<sup>4</sup> over an 18 month period, 347 requests for follow up of transfused babies were sent out. Of these, 252 samples should have been returned to the laboratory (excluding deaths; non-transfused babies; out of area babies and 12 already re-screened), but only 71 repeat samples were completed - 28% of the expected number.

#### Current Policy

##### Pre-transfusion samples

The initiative of taking bloodspot samples pre-transfusion, which was initially introduced in South East England, has been formal bloodspot programme guidance since 2008.<sup>2</sup> The Guidelines for Newborn Blood Spot Sampling state:

*"Where possible blood spots should be taken for SCD screening prior to blood transfusion."*

Guidelines for Newborn Blood Spot Sampling 2008:8  
UK Newborn Screening Programme Centre

On admission to neonatal intensive care units (or the equivalent), babies 5 days of age or less should have a single circle blood spot sample taken and marked as 'PRE-TRANSFUSION'. This sample should be attached to the routine 5-8 day bloodspot sample and **both** bloodspot cards sent to the newborn screening laboratory.

By taking an admission day sample the number of babies who require further intervention to obtain a valid sickle cell screening result is eliminated and as such this is a cost effective strategy, saving the considerable time and resources normally required for the follow up of transfused babies.

Introduction of this guidance for babies screened at South East Thames Screening Laboratory Partnership resulted in a reduction in the number of babies requiring post transfusion testing from 597 to 224.<sup>5</sup>



If extrapolated to the rest of the country, we would expect to reduce the number of repeat testing required to approximately 1,683 babies annually, a 51% reduction of the total number of 3,275 babies who had a blood transfusion in 2007/8 (Table 1 in [Appendix 1](#)).<sup>1</sup> This downward trend is well reflected in the number of transfused babies for 2008-9 which was 2,032 babies of a total of 670,284 babies screened.

### **Risk Management - DNA testing of transfused babies**

Babies who are not screened prior to having a blood transfusion are at considerable risk of being missed for sickle cell screening as previously highlighted. This also includes babies who have had an intrauterine blood transfusion. This risk is being actively addressed by the NHS Sickle Cell & Thalassaemia Screening Programme as the value of newborn screening for sickle cell disease is diminished if appropriate steps are not established to ensure that screening takes place and action ensues to follow up abnormal test results. **Failsafe** is a back-up mechanism, to supplement usual care, which ensures that robust systems are in place to:

- (i) identify when the usual processes have not been followed;
- (ii) initiate action for a safe outcome.

As a failsafe measure to ensure that transfused babies are offered appropriate screening, the Programme Centre has commissioned a service of DNA testing for babies who have not had a pre-transfusion bloodspot sample taken. **The process will identify babies with the sickle cell gene, regardless of transfusion state or gestational age, who require follow up and possible treatment.**

**This service is not aimed at replacing the pre-transfusion blood spot sample that should be taken from all babies admitted to neonatal intensive care units at less than 5 days of age. The current policy of taking a “PRE-TRANSFUSION” sample and sending this to the newborn screening laboratory along with the routine bloodspot sample taken on day 5-8 should continue. The service is a [safety net](#) for those babies who have not been included in the pre-transfusion sampling process.**

Testing of transfused babies is not equal to the newborn screening programme for sickle cell disease. It is a cost effective risk management alternative to the option of no screening for babies who have had a blood transfusion. It is anticipated that it **will eliminate the need for follow up of 90% of transfused babies**, in addition to those already tested pre-transfusion. Based on the data from the Newborn Screening Laboratories for 2007- 8, it is estimated that approximately 35 babies will have the presence of sickle cell haemoglobin identified in their bloodspot sample following DNA testing.<sup>1</sup> The majority of these babies will be carriers of the sickle cell gene.

### **Project Plan**

King's College Hospital (KCH) and Sheffield Children's Hospital (SCH) have been awarded the contract to provide sickle cell testing using DNA technology on bloodspot samples from transfused babies. This service will be introduced throughout England in November 2009.

The initial DNA testing period is for 2 years and if a review of the impact of the service is favourable, it is hoped to continue testing transfused samples as an integrated part of Newborn Screening for Sickle Cell Disease.

Both laboratories (KCH & SCH) have submitted a Gene Dossier to the Genetics Testing Network Steering Group for approval and inclusion in the portfolio of UK-GTN tests.<sup>1</sup>

---

<sup>1</sup> [http://www.ukgt.nhs.uk/gtn/Information/Services/Gene+Dossiers/Gene\\_Dossier\\_evaluation\\_process](http://www.ukgt.nhs.uk/gtn/Information/Services/Gene+Dossiers/Gene_Dossier_evaluation_process)

