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Newborn screening program for Sickle cell disease and Thalassemia

Procedure Guidance. Draft

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- The screening should be offered to all infants

• **INFORMED CONSENT:** An explanatory leaflet detailing the purpose, process and outcomes of newborn screening for sickle cell conditions must be provided to the parent(s) prior to screening. It should be explained by midwives during pregnancy and then again after delivery. In cases where the infant's parent(s) does not wish the child to be screened for sickle **, the decision to opt out of testing must be documented**.

• Information documented on the cord blood should be accurately and completely recorded in order to facilitate interpretation and delivery of results, and implementation of clinical care.

• It is especially important that information regarding blood transfusion prior to sampling is accurately documented to avoid the error of analyzing transfused red cells

- **SAMPLE**

Cord blood will be collected at birth, and posted to the neonatal screening laboratory within 24 hrs of collection. Samples may be stored at +40C prior to analysis**,** and can be expected to be stable for up to two weeks.

In occasional cases where there has been a delay in the blood being sent to the laboratory or if it has been kept in unsuitable conditions, excessive oxidation may occur rendering the sample unsatisfactory for analysis.

In order for the sample to be processed satisfactorily and to facilitate patient follow up, it is essential that the following are provided on the blood sample form

- Adequate demographics for the infant and the mother, including the baby's CPR number
- Indication if the child has been transfused
- The gestation of the infant

- If a multiple birth, state rank

- **SAMPLE ANALYSIS**

Newborn screening for sickle cell disorders, using HPLC can be reliably undertaken to detect the haemoglobin fractions present.

In the case of suspected abnormality, a second line test is used to confirm the presumptive diagnosis. Using this approach, the presumptive identification of haemoglobin variants obtained is accurate for clinical purposes.

It is important to note that unequivocal identification of haemoglobin variants can only be achieved by either protein sequence analysis (eg using mass spectrometry) or analysis of DNA extracted from blood.

Important to note for this screening programme, occasionally the presumptive identification of haemoglobin variant using screening methods may be incorrect since some variants give exactly the same results on screening.

No screening programme is 100% specific and sensitive as it is not a diagnostic service. This should not be the case with haemoglobins S, C, DPunjab, E and OArab. With any Hb variant misinterpretation should be minimal. However, it is important to note that careful wording of the reports issued is most helpful in order to avoid misleading information to colleagues and parents as to exactly what has been achieved from the screening.

In cases where there is a significant chance that the identity of the variant in doubt, it is important that no firm identity is reported until further testing is undertaken.

- **Responsibilities:**

1-The midwife in the maternity hospital is responsible for:

- informing the parent(s) of the reasons for testing.
- providing relevant information to parents
- offering the test, collection of the sample, labeling and sending off the cord blood sample after birth as soon as it has been taken
- obtaining informed consent or written notification if the parents wish to opt out of testing

Filling the form:

a. A specific form will be filled with the following information
b. **Baby**: CPR, name, address, telephone, nationality, date of birth and alive or still birth.
c. **Mother**: CPR, name, address, telephone, nationality, age, area of origin, gravida para, abortion, living, dead, maternity hospital, post natal health center, blood group, RH and genetic blood disease(G6PD, B.Thal, Alpha Thal., Sickle Cell).
d. **Father**: CPR, name, address, telephone, nationality, age, area of origin, blood group, RH and genetic blood disease (G6PD, B.Thal, Alpha Thal, Sickle Cell).
e. Mother and Father relationship.
f. A blood sample is taken from the baby which is then sent with the form to the laboratory.

2- The screening laboratory is responsible for:

• Documentation of the infant's demographics, specimen analysis and issuing of results within 2 weeks (14 days) of receipt of the sample

• reporting results of infants with sickle cell disorders to the genetic department responsible for the follow-up of affected infants

- MDIS Lab system **,**

a. Same screen used for student screening in the MDIS Lab system is used for the newborn screening, but another flag 'I' will be used for the newborn screening.
b. The CPR and name of the baby will be entered in the MDIS Lab system:
c. The hemoglobinopathy(HPLC) test results of the baby is entered in the MDIS Lab system.

The form will be sent to the Genetic Department

3- The coordinating centre/ (genetic department)

- (consisting of appropriate Health care professionals with relevant knowledge , skills and training) is responsible for:
- **In Genetic Department, the following information should be entered in the MS Access NPPHBD system by the secretary :**

a. Baby: Address, telephone, nationality, date of birth and alive or still birth.
b. Mother: CPR, name, address, telephone, nationality, age, area of origin, gravida para, abortion, living, dead, maternity hospital, post natal health center, and genetic blood disease, (G6PD, B.Thal. , Alpha Thal., Sickle Cell).
c. Father: CPR, name, address, telephone, nationality, age, area of origin, genetic blood disease(G6PD, B.Thal. , Alpha Thal., Sickle Cell).
d. Mother and father relationship.
e. The blood test results and the conclusion.

The genetic department is responsible for:

• informing parents of the positive results and arranging clinical follow up of infants with sickle cell disease
• informing parents of the results and arranging clinical follow up of infants with other potentially clinically significant conditions
• arranging repeat testing as indicated
-referring the affected infants to the pediatrician for treatment
• ensuring that infants are not lost to clinical follow-up before enrolment in a clinic
• reporting results of unaffected and carrier infants to the relevant child doctors, MCH department **through specific computer system.**

4- At the **MCH department**:
• providing information and counseling for the parents of infants who are normal, carriers, or have other benign conditions detected
• repeating the test if requested by the Coordinating centre
• confirming the diagnosis if required after 3 months.
• referring the newly diagnosed cases to the center

INTERPRETATION OF RESULTS
Results of haemoglobinopathy screening by hematologist are interpreted according to the different haemoglobin fractions present, which in unaffected infants are Hb F (as the major fraction) and Hb A. If the results of the first line screen show the presence of any abnormal fraction, second line testing must be undertaken.

REPORTING OF RESULTS
• A uniform approach is recommended.

• It is recommended for the Hb initials to be reported in the order of greatest to least percentage.

• The parents and doctors should be informed of all the outcomes of screening.
•Laboratories are responsible for sending results through computer to Genetic department – in a timely manner - for onward dissemination of results to doctors and parents.

Screen positive results should be dealt with immediately by the laboratory.

Action required for particular categories of results:

Infants with sickle cell disorders:

Results should be sent, by the laboratory, as a matter of urgency to the nominated genetic department which is the coordinating center, and confirmation of receipt documented. Parents and the child doctors should be informed by personal contact and in writing.

Infants with no abnormality detected:

Results should be provided in written form for the parent(s) of the child and the child's doctors

Infants heterozygous for a haemoglobin variant:

Results should be communicated to the parent(s) of the child and the child's doctors.

Infants found to have condition other than sickle cell disorder which requires follow up:

Results should be sent, by the laboratory, to nominated coordinating centre, and confirmation of receipt made. Parents and the child doctors should be informed by personal contact and in writing.

Genetic department, Hematology clinic and Child Health Computer systems/or equivalent should have links to laboratories to allow the notification of receipt of samples and the reporting of results.

FOLLOW-UP PROCEDURES

• **Infants with sickle cell disorders:**
Diagnostic testing should be undertaken on samples taken before 2 months of age, unless results are available from antenatal or other screening on the parents. Parental samples (where required) should also be tested at the same time. Samples for diagnostic testing for sickle cell disorders should be sent to a specialist laboratory, which has expertise in haemoglobinopathy analysis.

• **Other clinically significant conditions:**
Diagnostic testing (when required) should be undertaken on samples taken before 2 months of age, and it is recommended that parental samples should also be tested at the same time. Samples should be sent to a specialized laboratory which has expertise in haemoglobinopathy analysis.

• **Carriers of Common Haemoglobin Variants (Hb S, C, DPunjab, E, OArab):**
Using screening techniques, confirmation using second and third line testing can confirm the presumed identity of the haemoglobin variant, and it should not be necessary to take a further blood sample. Carriers are usually asymptomatic but can be at risk under particular high stress situations. It is helpful if their families are made aware of their carrier status and screening of parents offered.

• **Rarer Haemoglobin Variants:**
Most of these will be infants who are heterozygous for the rarer variants and will have no clinical or hematological manifestations. However, some rare variants, particularly unstable haemoglobins or those with altered oxygen affinity can produce clinical manifestations even in the heterozygous form. In order to establish the identity of the condition, further samples should be referred to a laboratory with expertise in haemoglobin analysis. Once the nature of the condition is established, medical follow up can be provided if necessary. These conditions are unlikely to be clinically important or common and should not be followed-up unnecessarily

• **Transfused Infants:**
Any infant who is known to have had a blood transfusion prior to testing must have a repeat test taken at least three months after the last transfusion. Any quantity of red cell transfusion, at any time (in utero or neonatally) should be regarded as significant and the test repeated.

• **Premature Infants:**

Hb A is normally detectable by 30 weeks gestation and is sometimes detected by 24 weeks. Results from premature infants should be interpreted with caution and premature infants who show no HbA need repeat testing to check for the presence of a sickle cell disorder or homozygous beta thalassaemia.
Family studies, DNA analysis, or re-evaluation during the first 1-2 years of life.

STANDARDS and QUALITY ASSURANCE

Timeliness: cord blood should be received in the screening laboratory by 24 hours after the birth of the baby.

The report should be sent by 1-2 weeks of age to enable arrangements to be made so that affected children can be vaccinated by eight weeks and attend a specialist clinic by 12 weeks of age

CPR Numbers: The form should have both the baby's **CPR** number, to ensure correct identification and to confirm coverage of the programme, and ideally the mother's **CPR** number to allow linkage with antenatal records.

Pre-maturity: Since the switch of globin production from gamma to beta is related to gestational age, infants born at less than thirty weeks gestation may need retesting six weeks after birth if the haemoglobin pattern is not clearly established

Blood Transfusion: Samples obtained from premature and other babies who have been transfused need to be repeated when all the transfused red cells have disappeared which will be 3 months after the last transfusion. Any amount of blood transfused should be considered significant and the child's test repeated.

Reports: will be available through the system

Storage of blood samples :
To study current legislation on the storage of human tissue.

Responsibilities:

1- **the midwife is responsible for :**
- **Informing the parnts of the reasons for testing.**
- **Providing relevant information to parents**

- **Offering the test, collection of the sample, labeling and sending off the cord blood sample after birth as soon it has been taken.**
- **Obtain informed consent or written notification if the parents wish to opt out of testing**

2- the screening laboratory is responsible for:

- **Documentation of the infants demographics, specimen analysis and issuing of results within 2 weeks (14 days) of receipt of the sample**
- **Reporting results of infants with sickle cell disorders to the genetic departments responsible for the follow-up of affected infants**
- **Reporting results of unaffected and carrier infants to the relevant child doctors,? Child health department through specific computer program**

3- the co-coordinating centre/ team (consisting of appropriate health care professionals with relevant skills and training) is responsible for:

- **Informing parents of the results and arranging clinical follow up of infants with sickle cell disease**
- **Informing parents of the results and arranging clinical follow up of infants with other potentially clinically significant conditions**
- **Providing information and counseling for the parents of infants who are carriers or have other benign conditions detected**
- **Arranging repeat testing as indicated by the laboratory. Ensuring that infants are not lost to clinical follow-up before enrolment in a clinic**

4- mother and child health

- **Informing parents of normal results and carrier status**

- **Reporting the test advised by coordinating centre to confirm diagnose after 3 month of ----if needed**

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