Directorate of Laboratory Medicine
Haematology Department
Oxford Road, M13 9WL

NHS Manchester University NHS Foundation Trust

Manchester Haemoglobinopathy Diagnostic Service

INDICATIONS FOR GENETIC DIAGNOSIS OF HAEMOGLOBINOPATHIES

Department of Haematology
Auto Lab CSB 2
Manchester Royal Infirmary, *Oxford Road*
Manchester M13 9WL
Telephone 0161 276 4803
Fax 0161 276 4654

Genetic diagnoses for Haemoglobinopathies for NW England will be coordinated through the Central Manchester and Manchester Children's University Hospitals NHS Foundation Trust (CMFT). Criteria for testing are detailed below. *Samples falling outside these indications will not be processed unless by prior agreement with the Haemoglobinopathy Clinical Team.*

Samples for testing must be labelled with full name, date of birth and NHS / hospital number and should be sent with appropriate referral form which must contain:

1. full patient demographic details (full name, date of birth, NHS / hospital number and address)

2. ethnicity

3. results of investigations (e.g. FBC, iron or ferritin levels and Haemoglobinopathy results)

4. evidence of patient consent

5. referring consultant, laboratory contact details and address for report

If Antenatal patient please send full details of partners results and ethnicity, if available.

On receipt of the sample the central laboratory will:

- Check sample labelling against specimen acceptance criteria.

Samples which fail specimen acceptance criteria will be rejected

- Check details on referring form and indication for testing against the agreed clinical criteria:
- Requests with incomplete information will be rejected, the referring laboratory will be contacted by fax to supply missing data, the sample will be stored for 2 weeks
- Samples that do not meet the testing criteria (see below) will be stored for 2 weeks and the referring laboratory informed by fax. There will be an opportunity for the referring haematologist to discuss the case with laboratory or medical staff at MRI
- Perform phenotypic analysis (HPLC and/or IEF)
- Perform genotypic analysis where indicated
- *The Manchester lab now performs a full PND service – samples are no longer referred externally*

Reporting: A combined phenotype/genotype report (where appropriate) will be sent from the Manchester Haemoglobinopathy Diagnostic Service with any necessary clinical interpretation.

Manchester Haemoglobinopathy Diagnostic Service

INDICATIONS FOR GENETIC DIAGNOSIS OF HAEMOGLOBINOPATHIES

INDICATIONS FOR MOLECULAR TESTING

1. Antenatal or pre-conceptual counselling

a) National Screening Committee guidance:

Maternal carrier state	Paternal carrier state	Further studies by DNA analysis
No abnormalities detected	Partner testing not required	None required
Any abnormal Hb	No abnormality detected	None required
Hb S	Hb S or Hb C	None required until PND
Hb S	Hb O-Arab, D-Punjab, Lepore, β thalassaemia	Send bloods for mutation confirmation of paternal carrier
Hb S	HPFH	Send bloods for mutation confirmation of paternal carrier state; if confirmed, PND is not indicated
Hb C	Hb S	None required until PND
Hb D-Punjab	Hb S	Send bloods for mutation confirmation for suspected D-
Hb O-Arab	Hb S	Send bloods for mutation confirmation of Hb O-Arab
Hb Lepore	Hb S, E, O-Arab, Lepore, β thalassaemia	Send bloods for mutation confirmation of Hb Lepore or Hb O-Arab
Hb E*	β thalassaemia, Hb Lepore,	Send bloods for mutation confirmation of β thalassaemia, Hb Lepore
β thalassaemia	Hb S, E, O-Arab, Lepore, β thalassaemia	Send bloods for mutation confirmation of β thalassaemia, Hb Lepore, Hb O- Arab
β thalassaemia*	Suspected α thalassaemia (MCH <25 pg)	Send bloods for mutation confirmation if of appropriate Mediterranean or SE Asian origin
suspected α^+ thalassaemia (MCH of 25–27pg)	Partner testing not required	None required
Suspected heterozygous α0 or homozygous α+ thalassaemia (MCH < 25pg) 1. Indian, Pakistani, African or North European, Middle Eastern	Partner testing not required	None required
2. South-East Asian, Eastern Mediterranean (Cyprus, Greece, Turkey, Sardinia), British** or unknown	Test partner and if: • MCH < 25 pg and from high risk area • MCH ≥ 25 pg and/or low risk	Send maternal and paternal bloods for mutation confirmation None required.

* = hidden risk of α thalassaemia ** = The NSC guidelines indicate that the partner need not be tested unless the patient is from a local high risk area (e.g. North-West England). PND = prenatal diagnosis

Manchester Haemoglobinopathy Diagnostic Service

INDICATIONS FOR GENETIC DIAGNOSIS OF HAEMOGLOBINOPATHIES

2. Carrier identification for genetic counselling purposes in non antenatal patients of appropriate age group.

• Diagnosis of unidentified Haemoglobin variants in pregnant women and/or partners (to link to variants identified in newborn screening programme)

3. Prenatal diagnosis

Prenatal diagnosis will be offered to couples at risk of having a child with any of the conditions that are listed below

Hb SS, Hb SC, Hb SD ^{Punjab}Hb S/β thalassaemia (β^o, β^+, δβ thal, Lepore) Hb S OArab Hb E/β

thalassaemia Hb Bart's hydrops fetalis (α^o /α^o) β thalassaemia major (except cases with silent or near silent maternal phenotype)

Parental samples, needed prior to PND procedure, will be arranged by the specialist nurses at the MSCTC

4. Newborn, Paediatric for genetic counselling and clinical management

- Genotypic investigation of B thalassaemia major/intermedia phenotype
- Investigation of Hb H disease (+ parents)
  Confirmation of Hb variant/ B thalassaemia, if not apparent from parental phenotypes.
- Unknown Hb variant analysis
- Sickle /HPFH

5. Adult haemoglobinopathy patients for genetic counselling and clinical management

- Genotypic investigation of B thalassaemia intermedia phenotype
- Investigation of abnormally raised Hb F levels (>5%)
- Confirmation of Hb variant/ thalassaemia if not apparent from phenotype

6. Investigation of possible alpha thalassaemia phenotype where clinically relevant (i.e. obviates need for further investigations)

These cases are extremely heterogeneous with many potential genetic defects. Testing is primarily indicated where it will impact on clinical management or where it is deemed important for genetic counselling. Family studies in such cases may be informative ie in compound heterozygous states and should be performed initially, if feasible.

- Thalassaemia intermedia phenotype (severe microcytic anaemia Hb > 2g/dl below normal range plus clinical features of haemolysis/splenomegaly, bone features, gallstones etc).
- Hb H disease
- Investigation of possible underlying alpha thalassaemia contributing to Anaemia of Chronic Disease when apparently iron replete

7 Investigation of unstable or high affinity haemoglobin

NB this list is not exhaustive. If in doubt about a referral please contact the

haemoglobinopathy clinical team on 0161 276 6772