

## Information Leaflet

### Haemoglobinopathy Carrier States (Genetics) for Health Professionals

#### Key Points

- Carriers for haemoglobinopathy do NOT usually require haematological referral or follow-up
- Refer if anaemia > 20g/l below normal range or splenomegaly or symptoms and iron deficiency excluded
- Blood counts for an individual tend to remain stable in adults so investigate if Hb drops from usual steady state
- Consider if genetic counselling information is needed
- Further advice and patient information can be obtained from the Manchester Sickle Cell and Thalassaemia Centre - 0161 279 3322

#### General Information

Inherited disorders of haemoglobin (haemoglobinopathy) may be detected on routine screening or in the course of hospital investigation. They should also be considered in all individuals with microcytic anaemia, particularly if there is no evidence of iron deficiency or red cell changes persist after adequate iron replacement. Although these conditions are more frequently associated with individuals of non-northern European origin, they may be found in all ethnic groups.

It is important to recognize carrier states for these haemoglobinopathies as they do not require iron treatment but the information may be important for genetic counseling for themselves, their partners (if planning pregnancy) or other members of their family. Women who have had pregnancies in recent years or partners of women with significant carrier states may have been screened as part of the national antenatal screening programme and may be aware of their haemoglobinopathy results. It is also useful to refer to historical results, for Hb, MCV and MCH, if available, as these remain relatively constant throughout adult life for a given individual; any significant deviation indicates an additional cause for anaemia such as iron deficiency.

Further information for health professionals and information for carriers may be found on the following websites and these contain useful genetic counselling information for those contemplating pregnancy.

- <https://www.gov.uk/guidance/sickle-cell-and-thalassaemia-screening-programme-overview>
- <https://phescreening.blog.gov.uk/2020/02/19/sct-genetic-counselling/>
- <https://www.gov.uk/government/publications/handbook-for-sickle-cell-and-thalassaemia-screening/prenatal-diagnosis-guidelines>
- <http://2000.apogi.info/>

**Leaflets and further advice are also available from the Manchester Sickle Cell and Thalassaemia Centre: Tel: 0161 274 3322.**

**Referrals for genetic counselling can be made by emailing**  
[mft.manchestersicklecell@nhs.net](mailto:mft.manchestersicklecell@nhs.net)

**Investigation of microcytic hypochromic (low MCV, MCH) indices where iron deficiency has been excluded or persists after treatment**

Consider the following conditions most frequently associated with microcytic hypochromic indices and send blood for haemoglobin screen and ferritin (if no result available):

- Alpha thalassaemia
- Beta thalassaemia
- Delta beta thalassaemia
- Haemoglobin E
- Other haemoglobin variants

Carriers for these haemoglobinopathies are clinically asymptomatic. Milder carriers may have a normal haemoglobin with minimal reduction in MCV and MCH while other carriers will have mild anaemia with more marked reduction in MCV and MCH. **Carriers for haemoglobinopathy do not need haematology follow up** however, individuals with more severe anaemia (> 20g/l below lower limit of normal) or those with symptoms or splenomegaly should be referred for a haematological review.

**Beta Thalassaemia**

Carrier states for beta thalassaemia are asymptomatic and have a mild anaemia often with marked microcytosis. Carriers should be referred for genetic counselling as offspring of beta thalassaemia carriers and partner carriers of beta thalassaemia or sickle cell or other haemoglobin variants may inherit the clinically significant Thalassaemia or Sickle Cell Disease respectively. Beta thalassaemia carriage is diagnosed on the finding of a raised Hb A2 level with other phenotypic evidence suggesting beta thalassaemia. In these cases a haemoglobinopathy card may be issued.

**Beta thalassaemia carriers do not need to be seen in the haematology clinic** unless there are atypical blood findings and concomitant iron deficiency has been excluded. Consider if genetic counselling is needed, particularly for individuals of childbearing age. See also above for information on accessing information for patients.

**Alpha Thalassaemia**

Alpha thalassaemia is usually suspected in a patient with a hypochromic, microcytic blood picture (with or without anaemia) where other causes for these findings such as beta thalassaemia or iron deficiency have been excluded.

**Alpha thalassaemia carriers do not need to be followed up in the haematology clinic** but should be referred for genetic counselling to the Manchester Sickle Cell and Thalassaemia Centre, if appropriate (see below).

Definitive diagnosis of alpha thalassaemia can only be made by DNA studies. This is not usually necessary except in certain circumstances (see below).

- There are 4 genes controlling alpha thalassaemia (2 on each chromosome) and the number of defective genes will dictate the clinical features:

- Persons with 1 or 2 defective genes are usually asymptomatic and do not need any further investigation or treatment. Iron treatment is not effective and should not be given unless concomitant iron deficiency is proven.

The only indication for further testing is in the antenatal context where it is important to distinguish those who have alpha zero (2 defective genes on the same chromosome) from those who have homozygous alpha + (2 defective genes on opposite chromosomes). The former will require partner testing to establish the risk to offspring of inheriting clinically significant alpha thalassaemia whilst the latter requires no further action. Alpha zero cannot be distinguished from homozygous alpha plus on blood indices alone. Alpha plus thalassaemia is extremely common being found in up to 30% of persons of African origin. It is also common in all parts of Asia, particularly in Southeast Asia. Alpha zero is found in some Mediterranean populations but its highest frequency is in individuals from southeast Asia. This forms the basis of the antenatal screening algorithm.

### **Issue of alpha thalassaemia reports**

Possible alpha thalassaemia may be picked up on routine testing or in the course of screening for haemoglobin disorders. In the antenatal or pre-conceptual counselling context, the national screening algorithm will dictate those women for whom partner screening is indicated. This will be on the basis of blood results and that woman's ethnic origin. Partner screening is indicated if the woman's MCH is < 25pg and she comes from a highrisk ethnic group. Partner testing will be arranged by the screening midwife in the ANC. Please contact Manchester Sickle Cell and Thalassaemia Centre for advice if pre-conceptual partner testing is recommended.

Outside the antenatal setting, reports may be issued as follows:

**Suggestive of alpha thalassaemia** – This is reported when hypochromic microcytic indices coexist but with normal ferritin levels and haemoglobin electrophoresis.

**Possible alpha thalassaemia/alpha thalassaemia cannot be excluded** – This will be reported when microcytic hypochromic indices are present, Hb electrophoresis is normal but iron levels are not available or are borderline low /unreliable. In this situation iron levels should be checked if no result available. If iron levels are low or borderline, a short course of iron should be given with repeat blood count after 4 weeks. If hypochromic microcytic indices persist despite adequate iron levels then alpha thalassaemia is likely. Iron deficiency should be investigated and managed in the usual way.

### **Sickle Cell Carrier Status (Sickle Cell Trait) +/- alpha thalassaemia**

Routine or emergency haemoglobinopathy screening will often identify individuals who are carriers for Sickle Cell. Such individuals will have both Hb A and Hb S present in approximately equal quantities, typically around 30-40%, depending on whether they also carry alpha thalassaemia. This is commonly encountered in persons of African origin since both carrier states have a high prevalence in this region. Concomitant alpha thalassaemia is suspected when microcytic hypochromic indices are present and will act to will lower the % of Hb S relative to Hb A. Raised Hb A2 levels are seen in sickle cell carriers and do not indicate coinheritance of beta thalassaemia (see below). Iron deficiency should be excluded.

Sickle Cell Carriers with or without coinheritance of alpha thalassaemia do not develop symptoms of Sickle Cell Disease and **do not need to be followed up in Haematology Clinics**. However, it is important that individuals receive genetic counseling for themselves or other members of their family in relation to the risk of any offspring inheriting a clinically significant disorder.

#### **Sickle Cell Beta Thalassaemia**

Coinheritance of sickle cell and beta thalassaemia typically produces Hb S levels greater than HB A. **Such individuals may have mild to severe sickle cell disease and require clinical follow up. Please refer to the haemoglobinopathy clinic.**