

## 1 ANTEPARTUM CARE

### 1.1 ANTEPARTUM CLINIC VISITS

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1.1.12 Haemoglobinopathies Screening and Referral  
Section B  
Clinical Guidelines  
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#### 1.1.12 HAEMOGLOBINOPATHIES SCREENING AND REFERRAL

##### AIMS

1. To identify and screen women and their partners at risk for haemoglobinopathies.
2. To offer genetic counselling to women and their partners who test positive for thalassaemia or sickle cell disease.
3. Provide referral for women to the Maternal Fetal Medicine for specialised multidisciplinary obstetric management when there is a confirmed haemoglobinopathy which carries risk for the woman or fetus.

##### BACKGROUND INFORMATION

Haemoglobinopathies are autosomal recessive disorders which imply that they must be inherited through both parents who may have the disorder themselves, or be carriers. Normal haemoglobin contains a haem molecule that combines with four globin chains, two of which are classified as alpha and two as beta chains.<sup>1</sup> The World Health Organisation estimates that approximately 5% of the world's population are carriers for haemoglobinopathies.<sup>2</sup>

##### THALASSAEMIA

Thalassaemia results from decreased synthesis of the globin chains in adult haemoglobin. It leads to ineffective erythropoiesis and increased haemolysis which results in inadequate haemoglobin content. The severity of the condition will depend on the number of abnormal genes.<sup>3</sup> The red cell indices show a reduction in mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) and sometimes anaemia.<sup>1</sup> It is classified as alpha ( $\alpha$ )-thalassaemia when there is absent or decreased  $\alpha$ -chain synthesis, or beta ( $\beta$ )-thalassaemia when there is absent or decreased  $\beta$ -chain synthesis.<sup>4</sup> Partner testing is required if a woman has a thalassaemia trait because if her partner also has a confirmed carrier trait it will pose risk for the fetus of major thalassaemia conditions. Inheriting the disease from just one parent is called thalassaemia minor, and usually causes no problems. The outcome of  $\alpha$ -thalassaemia major condition will result in fetal hydrops.  $\beta$ -thalassaemia major neonates are protected at birth by fetal haemoglobin, but as this wanes, increasingly severe anaemia develops leading to ongoing transfusions and associated complications.<sup>5</sup>

##### SICKLE CELL DISEASE

Sickle cell disease occurs when the structure of the beta globin chain is abnormal.<sup>1</sup> Defective genes produce abnormal haemoglobin beta chains resulting in Hb called HbS. Sickle cell disease (HbSS) occurs when abnormal genes are inherited from both parents. Sickle cells have increased fragility and a shortened life span of 17 days causing chronic haemolytic anaemia which leads to episodes of ischaemia and pain known as sickle cell crises.<sup>3</sup> A sickle cell trait is when a person inherits only one sickle cell gene and does not have disease.<sup>1</sup> Maternal effects from HbSS include pain, infections,

pulmonary complications, anaemia, pre eclampsia and caesarean section. The fetus is at risk for spontaneous abortion, pre-term birth, intra-uterine growth restriction and perinatal death.<sup>3, 6, 7</sup>

## AT RISK GROUPS FOR HAEMOGLOBINOPATHIES

Populations at risk for haemoglobinopathies include:

### Thalassaemia

- African<sup>2, 7</sup>
- South East Asian and Chinese<sup>2, 7</sup>
- Middle Eastern<sup>2</sup>
- Pacific Islanders<sup>2</sup>
- New Zealand Maori<sup>2</sup>
- Southern Europe/Mediterranean<sup>2, 7</sup>
- Indian subcontinent<sup>2</sup>
- Some northern Western Australian and Northern Territory Australian indigenous communities.<sup>2</sup>

### Sickle Cell Disease

- African<sup>4</sup>
- African American<sup>4</sup>
- Middle Eastern<sup>4</sup>
- Southern Europe/Mediterranean<sup>4</sup>
- Indian subcontinent<sup>4</sup>
- South American<sup>4</sup>
- Caribbean<sup>4</sup>

## EFFECT OF THALASSAEMIA TYPES IN PREGNANCY

TYPE OF THALASSAEMIA	GENE INHERITANCE	EFFECT
Alpha thalassaemia minor or $\alpha$ -thalassaemia trait	One or two defective $\alpha$ genes	Asymptomatic normally. May have mild anaemia. <sup>8</sup>
Beta thalassaemia minor or $\beta$ -thalassaemia trait.	One defective $\beta$ gene	Asymptomatic normally. May have mild anaemia. <sup>8</sup>
Alpha thalassaemia major (heterozygous alpha thalassaemia)	Three defective $\alpha$ genes	HbH disease (Chronic anaemia state).
Homogenous Alpha thalassaemia	Four defective $\alpha$ genes	Bart's disease / Hydrops fetalis <sup>7</sup>
Beta thalassaemia major Haemoglobin H disease	Two defective $\beta$ genes Three defective alpha genes	Severe anaemia. Require frequent blood transfusions. May result in death in early childhood. <sup>3, 8</sup>

**Note:** Ethnicity should not be presumed from a country, birth or surname. Detailed family history is more indicative of status.

## SCREENING ANTENATAL WOMEN FOR HAEMOGLOBINOPATHIES

Patient Information Pamphlets are available at the following link

<http://www.genomics.health.wa.gov.au/publications/index.cfm#pamphlets>

**Refer to flow chart at the end of this guideline.**

All antenatal women should be offered screening if they fall into these categories:

- Past history of unexplained anaemia
- Family history of anaemia (unknown cause) or haemoglobinopathy
- Belonging to an 'at risk' ethnic background for haemoglobinopathies.

**Or**

- Women who have no risk factors for haemoglobinopathies but blood results show a  $MCV \leq 80$  and  $MCH \leq 27$  and a normal Ferritin level.

**SCREENING AND REFERRAL PROCESS**

***Women with no risk factors for haemoglobinopathies***

Assess the FBP (full blood picture) and Ferritin levels (if done) of all antenatal women at the booking visit.

- Normal FBP – reassess FBP when the diabetes screening is ordered.
- Abnormal:
  - If the  $MCH \leq 27$  and the  $MCV \leq 80$  check Ferritin status:
    - If there is a low Ferritin status arrange treatment for iron deficiency anaemia.
    - If the Ferritin levels are normal, counsel the woman and arrange Haemoglobin studies (HPLC High Performance Liquid Chromatography) and FBP. Thoroughly assess family and partner history for risk factors.

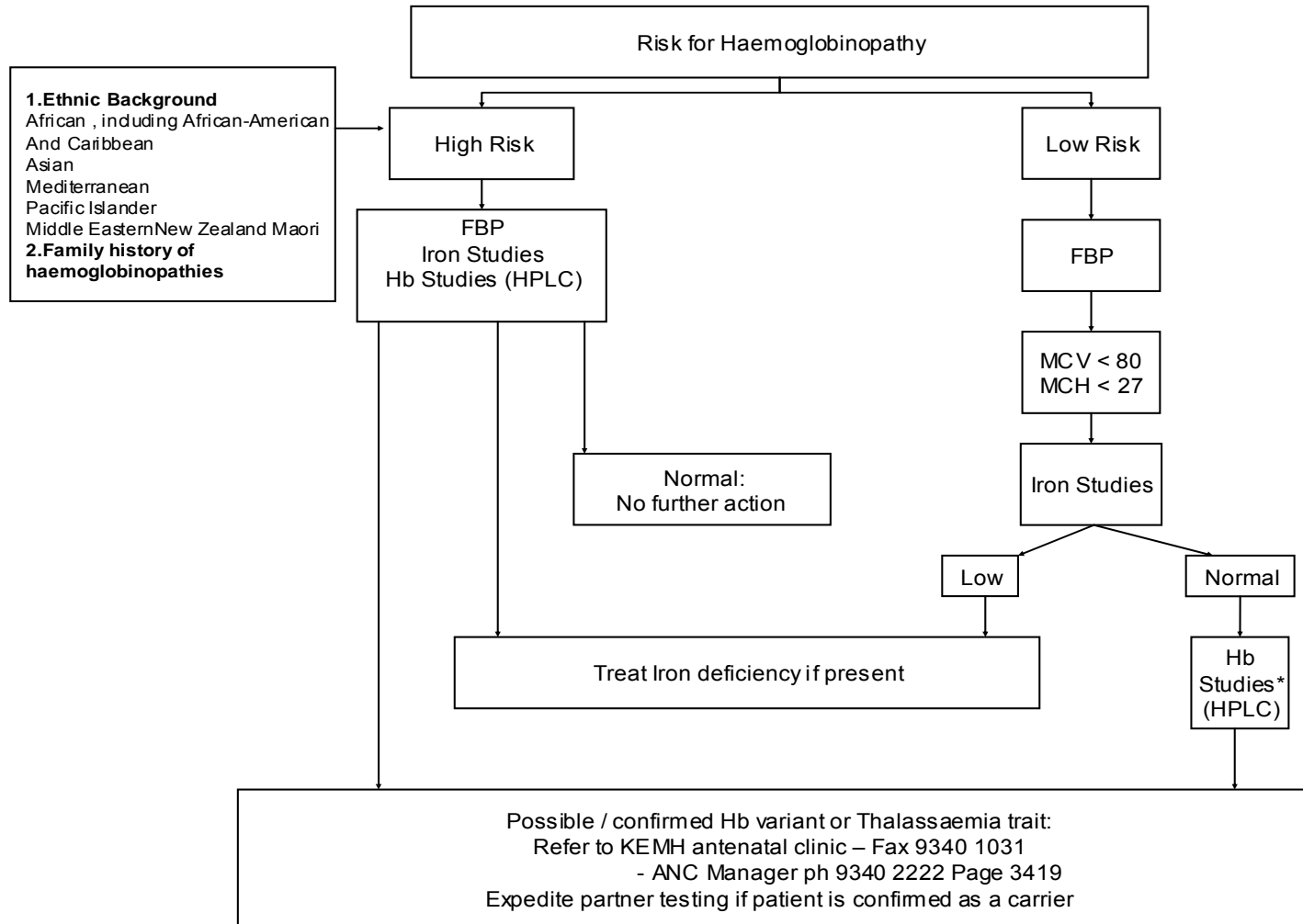
***Women who are at risk for haemoglobinopathies***

1. Assess FBP and Ferritin levels.
2. Confirm if she has had previous testing for haemoglobinopathies. Obtain a copy of results if already done. Assess if partner test has had testing and confirm status.
3. Provide counselling and, with maternal consent, arrange screening for haemoglobinopathies. If Ferritin levels are low initiate treatment for iron deficiency.
4. If the woman is attending a low risk midwives clinic and the Hb testing is abnormal, the woman should be referred to the Team Obstetric clinic for follow-up and counselling about the blood results. If the Haemoglobin studies results are normal the women may then continue antenatal care at the midwives clinic.
5. If the woman tests positive for a haemoglobinopathy, fax referral to the Maternal Fetal Medicine Haemoglobinopathy Coordinator (MFM Hb) (fax 93401060) and arrange testing for her partner as soon as possible. Partner testing may be initiated concurrently when the woman is tested according to gestation to provide faster results for the couple.
6. MFM Coordinator will review results in consultation with MFM Specialist to determine the risk to the fetus.
7. If test results confirm a high risk haemoglobinopathy condition impacting on pregnancy referral to Maternal Fetal Medicine for ongoing care will be arranged. This may also include genetic counselling, physician and haematologist involvement.
8. For couples with a known risk of significant haemoglobinopathy in offspring, refer directly to Maternal Fetal Medicine service or Genetic services.

## REFERENCES

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**INVESTIGATIONS OF PATIENTS FOR HAEMOGLOBINOPATHY**



- Hb studies can be requested as an add-on to the FBP