Protocol for Haemoglobinopathy Carrier Screening in Victoria

All women (and partners) planning a pregnancy or currently pregnant should be offered thalassaemia screening if not previously performed[1]

Arrange blood tests for patient:
[test partner at the same time if possible]

- FBE
- Hb electrophoresis
- Fe studies
- DNA studies (if indicated)*

Normal FBE & Hb electrophoresis
No further action, unless partner known to be carrier of non-deletional alpha mutation or 2-gene deletion alpha thalassaemia (in which case DNA testing is required)

Abnormal FBE
(MCV and/or MCH below or equal to the reference range)

AND/OR

Abnormal Hb electrophoresis

****Arrange blood tests for partner ASAP:**
(if not already done)

- FBE
- Hb electrophoresis
- Fe studies
- DNA studies (if indicated)*

Normal FBE & Hb electrophoresis in partner
Couple at low risk of child with severe haemoglobinopathy
Disclosure of carrier status to patient via GP, obstetrician or midwife***
Referral to genetic counselling service if patient concerned or confused

Abnormal FBE & Hb electrophoresis in partner

1. **URGENT Referral** to genetic counselling service for counselling & risk assessment
2. Couple <u>may</u> be at risk of child with severe haemoglobinopathy

<u>VERY IMPORTANT POINTS:</u>

1. *DNA studies (if indicated) MUST be put on the pathology form to ensure it is sent to the DNA lab in a timely manner if required
2. **Ensure you put the partner's details on the pathology slip so the lab can link the couple
3. ***Look out for DNA results from lab – may be done depending on patient's results. Refer for genetic counselling if any concern
4. DNA testing can take up to 2 months, occasionally longer for rarer mutations, so please order as early as possible
5. Where possible order testing for patient and partner at the same time if already pregnant
6. Rarely couples with normal haematology may be at risk of having a child with HbH disease and may not be detected via this screening protocol
7. If a DNA mutation is detected, discuss with patient the importance of sharing this information with family members
8. *Please refer over the page for what to look out for, common genotype combinations, and when to refer for genetic counselling*

<u>Monash thalassaemia genetic counselling: Tel –9594 2026. Fax (referrals) –9594 6022</u>
<u>If in doubt - CALL</u>

[1] Cunningham F, Bowden D, 2013: *Suggested protocol for pre-conceptual and antenatal carrier testing for haemoglobinopathies*, Thalassaemia Services Victoria, Medical Therapy Unit, Monash Medical Centre, Monash Health, Victoria, Australia (adapted)

Screening for Thalassaemia and Sickle Cell Disease in Victoria

Haemoglobinopathies, including thalassaemia, are inherited disorders of haemoglobin production. Collectively, they are the most common inherited conditions in the world. If not treated, symptoms of a severe haemoglobinopathy may include failure to thrive, severe anaemia, cardiomyopathy and shortened life span. Being a carrier is common in people from certain areas of the world, particularly the Mediterranean, South East Asia, and parts of Africa, but anyone could be a carrier.

Haemoglobinopathies are recessive conditions

- People have 2 pairs of alpha globin genes (4 copies) to produce alpha globin AND 1 pair of beta globin gene (2 copies) to produce beta globin.
- Carriers of haemoglobinopathies are usually healthy and have no symptoms.
- When both parents are carriers of a gene mutation in the SAME gene they may have a 1 in 4 chance of having a child with a severe haemoglobinopathy.
- ***Couples who are <u>both</u> carriers of a haemoglobinopathy should be referred for genetic counselling to discuss their risk and options for future or current pregnancies.***
- ***Pregnant carriers whose partners are not available for testing should be referred for genetic counselling.***

<u>What to look for in test results</u>

- Low MCV/MCH
- Abnormal band on Hb Electrophoresis
  - Low MCV/MCH will identify most carriers of alpha and beta thalassaemia and some globin variants
  - Carriers of alpha thalassaemia only will usually have normal Hb electrophoresis
  - Carriers of beta thalassaemia or beta variants usually have abnormal Hb electrophoresis
  - Carriers of sickle cell disease frequently have normal FBE results but abnormal Hb electrophoresis
  - Carriers of beta thalassaemia need DNA studies to see if they are also carriers of alpha thalassaemia
  - If one partner is carrier of a 2-gene deletion for alpha thalassaemia, then full DNA studies MUST be done on the partner, even if they have a normal FBE

<u>Beta thalassaemia:</u>

- **Beta thalassaemia major or intermedia** - change or deletion in both copies of their beta globin genes
- **Carriers of beta thalassaemia** (beta thalassaemia minor)
  - Often have low MCV and/or MCH and usually have raised HbA_2 on Hb electrophoresis

<u>Alpha thalassaemia:</u>

- **HbH disease:** Change or deletion of three copies of the alpha globin genes. Only one functional alpha globin gene
- **Bart's Hydrops Fetalis:** changes in or deletion of all 4 copies of alpha globin genes. Lethal condition with risk of <u>severe maternal complications</u>
- **Carriers of alpha thalassaemia** (alpha thalassaemia trait/minor):
  - Have a mutation or deletion in one or two copies of their alpha globin genes
  - MCV/MCH reduced (or may not be reduced if only one alpha globin gene altered or missing)
  - Normal Hb electrophoresis unless carrier of beta globin change as well
  - DNA studies required to determine nature and arrangement of changes and risk to couple. Some arrangements result in low risk of severe haemoglobinopathy, others lead to very serious conditions

<u>Haemoglobin Variants -</u> ***There are many other variants that can be identified, call for advice if detected***

<u>Sickle Cell (HbS)</u>

- **Sickle Cell Disease** –
  - HbS mutation in both beta globin genes, OR
  - Coinheritance of HbS and β-thal/ another structural variant → may cause severe disease
- **Carriers of sickle cell disease**:
  - Have an HbS mutation in one copy of their beta globin gene. Have one functional copy
  - Usually have normal FBE, detected on Hb electrophoresis

<u>Haemoglobin E (HbE):</u>

- **HbE/ β^0** - Could cause severe thalassaemia syndrome
- **HbE / HbE**: Usually asymptomatic or mild anaemia, unless co-inherited with alpha thalassaemia
- If both parents are carriers of an HbE mutation = low risk to have a child with a severe thalassaemia
  - **BUT** need to do DNA studies to ensure the parents are not also carriers of alpha thalassaemia