Haemoglobinopathy carriers

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
Haemoglobin AA	Normal haemoglobin	None	Normal haemoglobin seen in all populations	No interaction	Not applicable
Alpha (α^{+}) Plus Thalassaemia carrier	This is not clinically significant, although it may resemble iron deficiency anaemia with normal iron serum levels If carrier status is suspected antenatally then no further tests are recommended Not included in the screening programme in England	None	Most common haemoglobinopathy in populations world-wide	**Alpha zero thalassaemia**	**Haemoglobin H Disease (Hb H Disease)** Prenatal diagnosis (PND) is not indicated for this condition
Alpha (α^{0}) Zero Thalassaemia carrier	2 alpha (--/αα) gene deletion Reduced MCV & MCH May resemble iron deficiency anaemia with normal iron serum levels DNA required to confirm carrier status, as it cannot be diagnosed by routine screening methods Confirmation of carrier status as part of the antenatal screening programme in England is only indicated if both parents are from a high risk group	Paternal screening if both parents are from a high risk group Genetic counselling and DNA to confirm carrier status ONLY if results from both parents indicate they may be alpha zero thalassaemia carriers	China (including Hong Kong), Taiwan, Thailand, Cambodia, Laos, Vietnam, Indonesia, Burma, Malaysia, Singapore, Philippines, Cyprus, Turkey, Greece, Sardinia, unknown family origins	Alpha zero thalassaemia Offer couple prenatal diagnosis (PND)	Alpha thalassaemia major (Hb Barts Hydrops Fetalis)
				Alpha plus thalassaemia (Unlikely to be detected during antenatal screening as it not considered clinically significant)	**Haemoglobin H Disease (Hb H Disease)** PND is not indicated for this condition

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
Beta (β) Thalassaemia carrier	Elevated haemoglobin A_2 Reduced MCV & MCH Reduced production of ß (beta) globin chains May be misdiagnosed as iron deficiency anaemia Unless iron deficient, then no supplement required There are a range of ß thalassaemia mutations	Genetic counselling & paternal/partner screening is indicated Sometimes requires DNA to confirm carrier status Not diagnosed during routine newborn screening	Mediterranean Middle East South East Asian South Asian (China, Indonesia, Vietnam and other countries in the region) Caribbean African Occurs sporadically in all populations including White British	β thalassaemia Offer couple PND	βthal/βthal β thalassaemia major or **βthalassaemia Intermedia**
				Hb Lepore Assessment by specialist - offer PND if indicated	Lepore/ βthal May present as Thalassaemia Major or **Thalassaemia Intermedia**
				Hb E Assessment by specialist - offer PND if indicated	E/βthalassaemia may present as Thalassaemia Major or **Thalassaemia Intermedia**
				Delta beta (δβ) thalassaemia Assessment by specialist - offer PND if indicated	βthal/δβthal May present as Thalassaemia Major or **Thalassaemia Intermedia**
				O Arab Assessment by specialist	**O^{Arab}/βthalassaemia is usually** similar to **Thalassaemia Intermedia**
				Hb S Offer PND	S/βthalassaemia

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
Hb Lepore carrier (Hb A/Lepore)	Red blood cells are usually hypochromic and microcytic Occasional enlarged spleen	Genetic counselling Partner screening	Mediterranean (Greek, Italian)	βeta thalassaemia Assessment by Specialist - Offer PND if indicated	May present as Thalassaemia Major or **Thalassaemia Intermedia**
				Sickle cell (Hb AS) Assessment by specialist - Offer PND if indicated	**Hb S/Lepore**
Delta (δ) Beta (β) thalassaemia carrier (Hb A/δβ thalassaemia)	Red blood cells are usually hypochromic and microcytic Occasional enlarged spleen DNA to confirm diagnosis	Genetic counselling Partner screening	Mediterranean (Greek, Italian)	β thalassaemia Assessment by specialist - Offer PND if indicated	May present as Thalassaemia Major or **Thalassaemia Intermedia**
				Sickle cell (Hb AS) Assessment by specialist - Offer PND if indicated	**Hb S/δβ thalassaemia**
Hereditary Persistence of Fetal Haemoglobin carrier (Hb A/HPFH)	Usually 2% or less of total haemoglobin in adults It is not possible to distinguish Hb SS from Hb S/HPFH and S/β^0 thalassaemia in newborn screening	Genetic counselling Partner screening	Africans Caribbean	**Sickle cell (Hb AS)** Assessment by specialist	**S/HPFH** Does not usually require treatment
Haemoglobin E carrie (Hb AE)	Lysine substituted for glutamic acid, 26th point ß globin chain Red blood cells may be hypochromic and microcytic	Genetic counselling Partner screening	South East Asia (India, Bangladesh) South Asia (China, Vietnam, Thailand, Indonesia and other countries in the region) Caribbean	β thalassaemia Assessment by specialist - Offer PND if indicated	E/β thalassaemia may present as Thalassaemia Major or **Thalassaemia Intermedia**
				Sickle cell (Hb AS) Assessment by specialist	**Hb S/E Disease**

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
Haemoglobin D^{Punjab} carrier (Hb AD^{Punjab}) also called $D^{Los\ Angeles}$ Other types of Hb D are not usually clinically significant	Glutamine substituted for glutamic acid, 121 point, ß globin chain Important to identify D^{Punjab} from other Hb D's due to clinical interaction with Hb S	Genetic counselling Partner screening	Indian Pakistan Caribbean Occurs sporadically in all populations including White British)	Sickle haemoglobin (Hb S) Offer PND	Hb S/D^{Punjab}
Haemoglobin C carrier (Hb AC)	Lysine substituted for glutamic acid, 6th point, ß globin chain	Genetic counselling Partner screening	West African Caribbean	Sickle haemoglobin (Hb S) Offer PND	Hb S/C Disorder
Hb O^{Arab} (Hb AO^{Arab}) carrier Also known as Hb Egypt	Lysine substituted for glutamine at 121st point of the ß globin chain	Genetic counselling Partner screening	North Africa Saudi Arabia Bulgaria/Eastern Europe Eastern Mediterranean	**β thalassaemia** Assessment by specialist	O^{Arab}**/βthalassaemia usually** similar to **Thalassaemia Intermedia**
				Sickle haemoglobin (Hb S) Offer PND	S/O^{Arab}

Genotype	Comments	Action Required	Populations most likely to be carriers (but not exclusively)	Interaction with	Condition as a result of interaction
Sickle Cell Trait/Carrier (Hb AS)	May have intravascular sickling if oxygen tension excessively low (for example, during anaesthetic) Possible haematuria Possible increased risk of urinary infections in pregnancy	Genetic counselling Partner screening	African Caribbean South East Asians Mediterranean	β thalassaemia Offer PND	S/β thalassaemia
				Hb C Offer PND	Hb S/C Disease
				Hb S Offer PND	Sickle Cell Anaemia (Hb SS)
				Hb D^{Punjab} Offer PND	Hb S/D^{Punjab}
				Hb O^{Arab} Offer PND	Hb S/O^{Arab}
				Delta beta (δβ) Thalassaemia Assessment by specialist	**Hb S/δβ thalassaemia**
				Hb Lepore Assessment by specialist	**Hb S/Lepore**
				Hereditary Persistence Fetal Haemoglobin Assessment by specialist	**S/HPFH** Not usually treated but investigations required

Serious interaction **Less serious interaction** **Minimal clinical significance**

References

1. Bain BJ (2006) *Other significant haemoglobinopathies*. Haemoglobinopathy Diagnosis, 2nd Edition Blackwall Publishing Ltd
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3. NHS Sickle Cell & Thalassaemia Screening Programme (2012) *Handbook for Laboratories. 4th Edition.* https://www.gov.uk/government/publications/sickle-cell-and-thalassaemia-screening-handbook-for-laboratories
4. Ryan et al on behalf of the British Committee for Standards in Haematology (2010) *Significant haemoglobinopathies: guidelines for screening and diagnosis.* Blackwall Publishing Ltd. British Journal of Haematology149, 35-49 http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2009.08054.x/epdf