α-thalassemia

1 in 9,000 births — α-thalassemia
1 in 55,000 births — ß-thalassemia

Frequency of carriers is higher in Africa, Asia (south and southeast), Mediterranean and Middle East.

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Handouts and references available at **www.stevenchan.us/alphathal**

CHROMOSOME 16	HEMOGLOBIN PRODUCED	SYMPTOMS & LABS	MANAGEMENT
Four genes control α-globin chain synthesis. **Normal.**	95% HbA $\alpha_2\beta_2$ 2% HbA_2 $\alpha_2\delta_2$ 2% HbF $\alpha_2\gamma_2$	Normality.	No therapy required.
1 gene is deleted in **α-thalassemia minima, α-thalassemia-2 trait, silent carrier of α-thalassemia**.	HbA $\alpha_2\beta_2$ HbA_2 $\alpha_2\delta_2$ HbF $\alpha_2\gamma_2$	**Asymptomatic.** Slight hypochromia. Slight microcytosis. Dx only by DNA analysis.	No therapy required.
2 genes are deleted in **α-thalassemia minor, α-thalassemia-1 trait.** trans African cis Asian	↓ HbA $\alpha_2\beta_2$ ↓ HbA_2 $\alpha_2\delta_2$ ↓ HbF $\alpha_2\gamma_2$	**Hypochromia.** **Microcytosis.** **Target cells.** MCV < 80 fL.	No therapy required.
3 genes are deleted in **Hemoglobin H disease.**	↓ HbA $\alpha_2\beta_2$ ↓ HbA_2 $\alpha_2\delta_2$ ↓ HbF $\alpha_2\gamma_2$ 5 – 30% HbH $-\beta_4$	**Microcytic. Target cells.** HbH can't release O2 to tissues, because affinity is greater than HbA + HbH insoluble → Precipitates form inclusion bodies. → **Chronic hemolytic anemia** (hepatosplenomegaly, indirect hyperbilirubinemia, ↑LDH, ↓haptoglobin, ↓leg ulcers) → **Neonatal jaundice, occasionally hydrops fetalis.**	Most don't require chronic transfusion in 1st decade of life. **Splenectomy, transfusion** in 2nd, 3rd decade of life. **Avoid oxidants that may exacerbate HbH** (e.g. antimalarials, some sulfa drugs).
All 4 genes are deleted in **Hb Barts.**	~~HbA $\alpha_2\beta_2$~~ ~~HbA_2 $\alpha_2\delta_2$~~ ~~HbF $\alpha_2\gamma_2$~~ Hb Barts $-\gamma_4$	**Hydrops fetalis:** High output heart failure → excess fluid accumulation → fetal demise, neonatal mortality.	Almost always lethal in utero. Consider therapeutic termination of pregnancy in mothers at risk. **Chronic intensive hypertransfusion, iron chelation, hematopoietic cell transplantation.**

Risk for producing offspring with **Hb Barts.**

Both HbH and Hb Barts can't release O2 to tissues → ischemia.