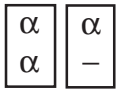
The 4 alleles for the α globin chain of hemoglobin are inherited in pairs.

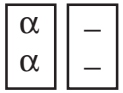
1 gene deletion = silent carrier



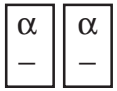
- asymptomatic
- may see small amount of Hb Barts* (γ_4) at birth
- normal red cell indices
- detected only by DNA methods

2 gene deletion = α-thalassemia trait

(effects of carrying either configuration are the same)



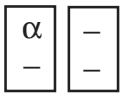
(cis)
common only in Asians



(trans)
common in African-Americans

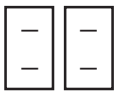
- mild anemia
- small red blood cells (low MCV)
- Hb Barts at birth
- difference between cis and trans becomes important when considering inheritance

3 gene deletion = hemoglobin H disease



- moderate to marked anemia
- very small red blood cells
- Hb Barts present at birth replaced by Hb H (β_4)

4 gene deletion = hydrops fetalis



- extreme anemia produces congestive heart failure, edema in utero
- stillbirth or early neonatal death

**** Hb Barts (γ_4): Because of the lack of α chains to pair with γ chains in the fetus to form fetal hemoglobin ($\alpha_2\gamma_2$), the γ chains form the tetramer Barts (γ_4). Disappears at 3-6 months of age.***

The thalassemias are hereditary anemias due to the underproduction of a given type of globin chain. Alpha-thalassemia is thalassemia due to a deficiency of alpha chains. The usual cause is deletion of alpha genes.

Diagnosis

Alpha-thalassemia should be suspected in an individual with unexplained microcytosis (with or without anemia) especially if Asian or if a fast-moving hemoglobin is found by electrophoresis. In an infant this fast-moving hemoglobin is usually hemoglobin Barts, a hemoglobin consisting of only gamma chains and indicative of deletion of 1, 2 or 3 alpha genes. In an older child or adult, the fast-moving hemoglobin is usually hemoglobin H, a hemoglobin consisting of only beta chains and indicative of 3 alpha gene deletions.

Samples for testing should be kept at room temperature and electrophoresed promptly since fast-moving hemoglobin may precipitate if stored or placed at 4°.

Treatment

The one- and two-gene deletion types of alpha-thalassemia, are asymptomatic and require no treatment. Individuals with the three-gene deletion type, called hemoglobin H disease, may require transfusion when the anemia is exacerbated by infection or other causes. Oxidant drugs may cause hemolysis and should be avoided. Hypersplenism may result from excessive blood cell accumulation, may aggravate the anemia and may be relieved by splenectomy.

Counseling

An Asian with microcytosis without elevated hemoglobin A_2 should have a test for iron deficiency. If not present, alpha-thalassemia is likely. If both partners have this picture, the couple may be at risk for a child with hemoglobin H disease or hydrops fetalis. The hemoglobin H disease risk possibility also exists for an Asian couple if one is microcytic due to two-gene deletion (cis), and the other has normal red cell indices and one-gene deletion α thalassemia. Family studies and DNA diagnosis may be needed to determine the number of alpha genes present.

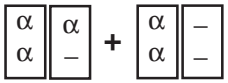
Prenatal Diagnosis

There is disagreement about whether hemoglobin H disease is severe enough to justify termination of pregnancy. However, if the fetus is shown to have four gene deletions, termination should be offered because most such children are stillborn or live only briefly and because delivery may be complicated by excessive fetal size due to edema secondary to fetal heart failure.

INHERITANCE

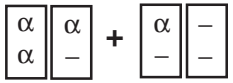
A pregnancy is at risk for hemoglobin H disease (3 gene deletion) if :

a) one parent has 1 α gene deletion and the other parent has 2 α gene deletion (cis)



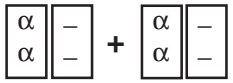
or

b) one parent has 1 α gene deletion and the other parent has hemoglobin H disease



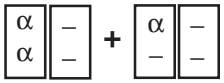
A pregnancy is at risk for Hydrops Fetalis if :

a) both parents have a 2 α gene deletion (cis)



or

b) one parent has a 2 α gene deletion (cis) and the other parent has hemoglobin H disease



The variations of alpha thalassemia have been discussed here. It must be noted that these variations can be combined with beta thalassemia or an abnormal hemoglobin such as hemoglobin E. The traits and diseases produced by such combinations may have mild or severe health consequences.

UNIVERSITY OF
ROCHESTER
MEDICAL CENTER

Division of Genetics
University of Rochester Medical Center
601 Elmwood Avenue
Box 641
Rochester NY 14642
(716) 275-4602

Visit our website:

www.urmc.rochester.edu/genetics

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α THALASSEMIA

Facts for Physicians