

# Arizona Hemoglobin Bart's Fact Sheet for Health Care Providers

## Hemoglobin Barts

Your patient has been found on the Arizona Newborn Genetic Screen to have a hemoglobin electrophoresis pattern consistent with "FA Bart's". The acronym stands for the hemoglobin species present in the baby's blood in descending order of prevalence. The F designates fetal hemoglobin ( $\alpha_2 \gamma_2$ ), A denotes hemoglobin A ( $\alpha_2 \beta_2$ ) and Bart's represents hemoglobin Bart's, a tetramer of  $\gamma$ -globin molecules ( $\gamma_4$ ). Hemoglobin Barts ( $\gamma_4$ ) appears in the newborn when one or more of the 4 human  $\alpha$ -globin genes are missing. The relative over abundance of  $\gamma$ -globin molecules leads to  $\gamma_4$  production and the diagnosis of Hemoglobin Barts.

Alpha thalassemia is caused by deletions of the alpha globin genes on chromosome 16. Normal individuals have 4 copies of the gene with 2 on each chromosome. It is possible to lose 1 to 4 of these genes. The presence of hemoglobin Bart's on newborn screen usually suggests that the infant is missing at least 1 alpha gene.

<b>*Usual Genotypes</b>	<b>Alpha-Globin Gene Deletions</b>	<b>Clinical Features</b>
$\alpha\alpha/\alpha\alpha$	0	Normal
$-\alpha/\alpha\alpha$	1	Silent Carrier
$--/\alpha\alpha$ or $-\alpha/-\alpha$	2	$\alpha$ -thalassemia trait
$--/-\alpha$	3	Hb H Disease
$--/--$	4	Fetal Hydrops

\*  $\alpha$  indicates presence of  $\alpha$ -globin gene. – indicates deletion of  $\alpha$ -globin gene

### **The silent carrier: One deleted Alpha Gene**

Neonates and children with three functional alpha genes have a complete or nearly completely silent phenotype. The red cell indices are normal and remain so for life. When only one a gene is non-functional, the hemoglobin Barts percentage is usually 1-2% in the newborn, and is not detectable when the fetal hemoglobin synthesis stops at 6 months of age. As the newborn matures, the red cells can rarely exhibit a reduced MCV, MCH, but will show normal HBA2 and F levels if the hemoglobin electrophoresis is repeated. This condition is clinically benign, and these patients require no other evaluation or special health care.

### **Alpha thalassemia trait: Two Deleted Alpha Genes**

Neonates and children with only 2 functional alpha genes will show alpha thalassemia trait. In the newborn period, Hemoglobin Barts is detected in the range of 5-6%. Most alpha thalassemia carriers will be mildly anemic, won't respond to iron therapy, and show mildly abnormal red cell indices. There is no specific treatment for the carrier state, but genetic counseling should be considered later in the child's life as it is possible that offspring could develop Hemoglobin H or hydrops. Individuals from SE Asia will often have the genes deleted from the same chromosome (*cis* mutation) while those of African heritage will have genes deleted from both chromosomes (*trans* mutation).

### **Hemoglobin H Disease: Three Deleted Alpha Genes**

Hemoglobin H disease occurs when there is only one functional gene, and these individuals can have a mild to moderate thalassemia. Most patients are anemic and develop splenomegaly although the clinical manifestations can be variable. These children would require care at a pediatric hematology/oncology center for moderate to severe symptoms.

### **Fetal Hydrops: All Four Alpha Genes Deleted**

This is also known as alpha thalassemia major. This is rarely compatible with life unless detected early. Those patients would be transfusion dependent, but death usually occurs in utero or in early infancy unless detected prenatally.

### **Follow-Up Recommendations:**

At 2-3 months, examine infant for splenomegaly and do a CBC. If normal and hemoglobin electrophoresis did not report abnormal hemoglobin other than Bart's then Hemoglobin H disease is unlikely and no further work-up is necessary until 9-2 months. If CBC or exam are abnormal, please consult a pediatric hematologist.

Between 9-12 months check CBC and reticulocyte count. If this is normal, then the child likely is a silent carrier. No further work-up of the child is necessary. If infant is microcytic, do iron studies and treat with 3-6 months of iron if found to have iron deficiency. If the microcytosis resolves with iron therapy, then the child is likely a silent carrier and needs no further evaluation. If the patient has persistent microcytosis, then they likely have alpha thalassemia trait.

The parents of a child with hemoglobin Bart's should also have CBC's performed, particularly if parents are of Asian ancestry. If the parents are microcytic, then further genetic testing and counseling should be done as there may be a risk of Hemoglobin H disease or hydrops in future children.

A diagnosis of a silent carrier or alpha thalassemia does not necessarily constitute a reason to refer your patient to a pediatric hematology/oncology center. However, should questions or other circumstances arise in the lives of the affected children, **for consultation contact Dr. Brenda Wittman or the pediatric hematologist on call at the University of Arizona School of Medicine at (520) 626-8278 or through Physician's Resource Service at (520) 694-5868.** Parents of this child may be directly referred for free counseling, screening, and educational services from the Sickle Cell Anemia Society of Arizona.