

## **The Role of Hemoglobin Barts in Umbilical Cord Blood Harvest & Transplantation**

The abnormal hemoglobin present during fetal development in individuals with four-gene deletion alpha-thalassemia was characterized at St. Bartholomew's Hospital in London and hence was named "hemoglobin Barts (Hb Barts)." In the homozygous state, when all four alpha-globin genes on chromosomes 16 are affected, no normal fetal or adult hemoglobin can be produced and the fetus becomes profoundly anemic in utero. This typically leads to stillbirth or death soon after birth due to severe hydrops fetalis accompanied by pulmonary hypoplasia and cardiac failure. Various heterozygous states can also produce detectable levels of Hb Barts, but with less dramatic clinical manifestations. These variants can be detected and quantified in umbilical cord blood (UCB) in proportions indicating one-, two- or three-gene deletion alpha-thalassemia, respectively representing silent carrier, thalassemia trait, and Hemoglobin H disease states. Silent carriers, the largest group with Hb Barts at birth, have a normal CBC, no clinically detectable problems and less than 5% Hb Barts present in cord blood sample. Individuals with alpha-thalassemia minor (or trait) have a very mild microcytic anemia but no other clinical problems, and express 5 to 10% Hb Barts in cord blood. One- and two-gene alpha-globin deletions are very common in African, Mediterranean and Asian populations, ethnic groups targeted for cord blood bank inventories.

Sixteen UCB products containing Hb Barts at levels consistent with either one or two alpha-gene deletions were exported for stem cell transplant from the St. Louis Cord Blood Bank. Survival of recipients receiving Hb Barts-containing units was not significantly different from those receiving cord products with normal newborn hemoglobin electrophoretic patterns ( $P = .5707$ ). To further evaluate the effect of transplanting units with Hb Barts variants, we propose an Institutional Review Board-approved study to evaluate erythropoiesis and the disappearance of fetal hemoglobin variants at designated post-transplant time points in patients who have been transplanted with these products.

In deliveries where the infant exhibits symptoms of hydrops fetalis, obvious perinatal complications would preclude cord blood harvest for the intended use of allogeneic transplantation. Considering the need for these unique and diverse HLA types, criteria for banking should allow inclusion of UCB units with Hb Barts content of less than 10% based on immunoelectrophoretic patterns. These units should pose minimal additional risk in transplantation and increase the ethnic diversity of bank inventories. Additionally, since recipients' genetic material remains intact after transplantation, they cannot pass these variant hemoglobins to their children.