

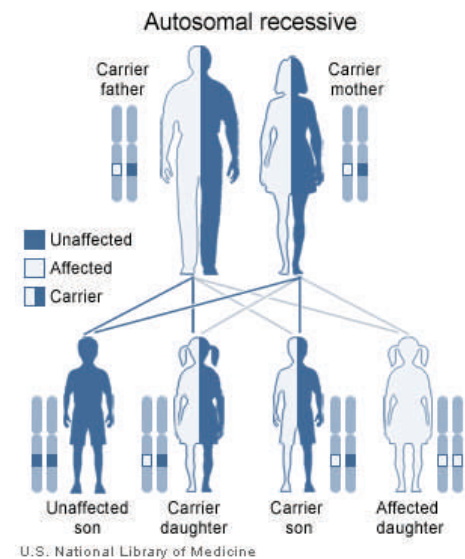
HEMOGLOBIN D DISEASE

Hemoglobinopathy screening in Utah identifies infants with hemoglobin disorders. Isoelectric Focusing (IEF), a screening process, separates, identifies, and quantifies each type of hemoglobin present in a sample. At birth there is normally more fetal hemoglobin (Hb F) than adult hemoglobin (Hb A) and is reported as FA. Infants with hemoglobin D disease have hemoglobin D (Hb D) with no Hb A. The IEF pattern of FD indicates hemoglobin *disease*. Abnormal IEF screens are validated by Hb fractionation using High Performance Liquid Chromatography (HPLC), which shows the hemoglobin pattern with somewhat more accuracy.

Genetics and Heredity

Hb D is an inherited autosomal recessive variation of Hb A that occurs in the beta (β)-globin protein chain of Hb A. The formation of Hb D occurs by substitution of glutamic acid for glutamin at codon 121 of the β -chain. Hemoglobin D disease (Hb DD) occurs when an infant inherits two copies of the Hb D variant gene, one from each parent. If both parents have the Hb D trait, there is a 25 percent chance with each pregnancy that the child will be born with Hb DD. Disease with no Hb A may have either homozygous Hb DD or heterozygous Hb D/ β -thal. Either diagnosis is associated with few clinical manifestations. The best method to distinguish the results is to test both parents.

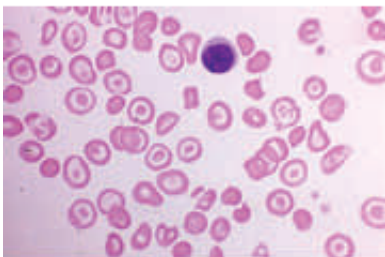
There are several Hb D variants. Hb D-Punjab, also known as Hb D-Los Angelese after the city where it was first discovered, substitutes glycine for the glutamic acid at codon 121 of the β -chain. Another variant, Hb Ibadan, substitutes lysine for the normal threonine at condon 7.



Prevalence

Hemoglobin D is the fourth most common hemoglobin variant, which developed as a response to the selective pressure of malaria. It is most often found in people living in India, Pakistan, England, Ireland, Holland, Australia, China, Iran, Turkey and their descendants. Homozygous Hb DD is rare and a relatively mild disease. Heterozygous Hb D/ β -thal is more common and more serious.

Pathophysiology



The following manifestations of hemoglobin D disease may be observed:

- Target cells
- Occasional spherocytes
- Microcytosis
- Hypochromia
- Mild hemolytic anemia
- Decreased osmotic fragility
- Reduced oxygen affinity

Homozygous Hemoglobin D:

Hemoglobin D disease is usually clinically silent with no special treatment required. A mild hemolytic anemia usually develops in the first few months of life as the amount of fetal hemoglobin decreases. Individuals with homozygous Hb D disease may be asymptomatic or the following may occur:

- Mild hemolytic anemia
- Mild to moderate splenomegaly

Vaso-occlusive episodes with accompanying complications are not a feature of Hb D disease. Decreased mean corpuscular volume (MCV) facilitates passage of RBCs through the microcirculation.

Heterozygous Hemoglobin D/Beta (β)-thalassemia:

Infants with heterozygous Hb D/ β -thalassemia may be asymptomatic and have mild to moderate hemolytic anemia depending upon the degree of β -thalassemia affecting the A gene. It usually develops in the first few months of life as the amount of Hb F decreases and Hb D increases. Those with Hb D/ β + -thalassemia have some Hb A and are more likely to have mild to moderate anemia and a non-palpable spleen. Children with hemoglobin D/ β^0 -thalassemia syndrome have no Hb A, exhibiting symptomatic anemia with splenomegaly and may have a moderately severe clinical disorder. Because RBC indices are abnormal in Hb D/ β -thalassemia, iron deficiency may develop.

Essential Steps

1. Inform the family of confirmed Hb D disease or Hb D/ β -thalassemia; explain the possible complications and interventions.
2. If hemoglobin D disease is present, it is important to ensure that the infant does not also have beta-thalassemia. A CBC with smear at 6 to 9 months of age will identify any of the β -thal components. If medical concerns arise or the infant is symptomatic, complete the CBC with smear earlier.
3. If iron deficiency is suspected serum iron levels, iron binding capacity, and percent saturation may need to be assessed.
4. Consult with a pediatric hematologist regarding patient evaluation and possible disease management.
5. Consider family referral to a genetic counselor.

Pediatric Hematology

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