The hemoglobinopathies, including sickle cell disease, alpha and beta thalassemia, are the most common single-gene disease in the world. Hemoglobinopathies affect hemoglobin production and function and are usually identified as a pattern of globin chains present in the blood. It is estimated that 5% of the world’s population is a carrier of a clinically important hemoglobinopathy. The hemoglobinopathies are usually transmitted as autosomal recessive traits, and each parent must have at least one affected allele in order for a child to be affected. Since most of the mutations that occur, the hemoglobinopathies are extremely heterogeneous disorders and represent a wide range of clinical phenotypes.

Six different types of globin chains are found in normal human hemoglobin: alpha (α), epsilon (ε), gamma (γ), delta (δ), beta (β), and theta (θ). Normal adult hemoglobin (HbA) has a tetrameric structure composed of two α and two β chains. This type of hemoglobin comprises approximately 97% of total hemoglobin in normal adults, while less than 2% of total adult hemoglobin is comprised of hemoglobin A2, which contains two α and two δ chains. The presence of fetal hemoglobin (HbF), which is made up of two α and two γ chains and comprises 50-85% of hemoglobin in newborns but declines after birth with normal adult hemoglobin, is expected to follow a decreased gestational age. Another study by Tan et al. removed pregnancies with additional gestational risk factors.

Pregnancies with sickle cell trait are at an increased risk for preeclampsia. American Journal of Obstetrics and Gynecology (1990); 33:19-21. 


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Hemoglobin is the oxygen-carrying molecule in red blood cells. The α2 chains are encoded by a gene cluster on chromosome 16. The β2 chains are classified as thalassemia.

Quantitative changes causing decreased synthesis of globin chains. This type of globin abnormality is typically associated with anemia. 

Qualitative changes in the structure of globin, such as sickle cell anemia.

Thalassemia syndromes are due to a deficiency or absence of one or more of the different types of globin chains. Some of the most common types of thalassemia are thalassemia major, thalassemia intermedia, and thalassemia minor. Thalassemia major is characterized by a complete absence of one of the globin chains, resulting in a severe anemia. Thalassemia intermedia is characterized by a partial absence of one of the globin chains, resulting in a milder anemia. Thalassemia minor is characterized by a decreased production of one of the globin chains, resulting in a mild anemia. Other forms of thalassemia include beta-thalassemia major, beta-thalassemia minor, and beta-thalassemia intermedia.

The presence of two mutations on separate chromosomes (ex. α-/α-).

The method by which hemoglobin variants are separated on a gel by exposing them to a pH gradient.

The method by which hemoglobin variants are separated by placing on a filter paper or gel and exposing them to a charge gradient.

The presence of two mutations on separate chromosomes.

The presence of two mutations on separate chromosomes (ex. α-/α-).

Thalassemia syndromes are due to a deficiency or absence of one or more of the different types of globin chains. Some of the most common types of thalassemia are thalassemia major, thalassemia intermedia, and thalassemia minor. Thalassemia major is characterized by a complete absence of one of the globin chains, resulting in a severe anemia. Thalassemia intermedia is characterized by a partial absence of one of the globin chains, resulting in a milder anemia. Thalassemia minor is characterized by a decreased production of one of the globin chains, resulting in a mild anemia. Other forms of thalassemia include beta-thalassemia major, beta-thalassemia minor, and beta-thalassemia intermedia.
Hb electrophoresis is normally used for routine screening. It requires no special equipment and is very inexpensive. However, it does not provide additional genetic information for the other types of abnormal hemoglobins. The diagnosis of sickle cell trait (Hb S) is made by performing hemoglobin electrophoresis or isoelectric focusing (IEF) with the presence of Hb S and Hb A, with Hb A representing a greater percentage than Hb S. The MCV and MCH are generally normal in sickle cell trait. The clinical features of thalassemia and sickle cell disease vary widely and researchers continue to identify additional genetic factors that modify the phenotypes of these conditions.

Beta thalassemia

Beta thalassemia is due to impaired production of β-globin chains resulting in an excess of γ-globin chains. Patients with β-thalassemia trait (Hb A2 > 4.5%) may have findings on routine testing similar to those seen in sickle cell trait (Hb S and Hb A present with Hb A > Hb S), but the MCV and MCH are lower. β-thalassemia trait is inherited as an autosomal dominant trait.

Alphas thalassemia

Alphas thalassemia is a group of disorders due to impaired production of the α-globin chains and may lead to an excess of β-globin chains. β-thalassemia trait is inherited as an autosomal dominant trait.

Why Should Screening be Performed? Early detection of sickle cell anemia or thalassemia means a child does not have to wait for the disease to begin before care can be started. However, the presence of a genetic marker for these disorders does not always mean the condition will be expressed. It is important to note that genetic markers are not always present in people with these disorders. The presence of genetic markers in the parents is always accurate as individuals may be from mixed ethnic backgrounds. Healthcare providers should be familiar with the risk factors for these conditions as they are associated with life altering or life threatening medical sequelae and/or chronic illness.

Recommends For Screening in Pregnancy

1. Individuals of African, Mediterranean, Caribbean, Middle Eastern, and Central American descent should have screening performed at least once during pregnancy. 
2. Individuals of other ethnic backgrounds should have a blood test performed. If the MCV is low this should be followed by an Hb electrophoresis or by a high performance liquid chromatography (HPLC) test.
3. When there is a family history of thalassemia, both parents should be screened for the Hb trait.
4. Couples at risk for bearing a child with sickle cell disease or thalassemia should be offered genetic counseling to review testing options and reproductive options.
