Defects of Hemoglobin

Hemoglobin S

HbS is the predominant form of hemoglobin in sickle cell patients which has a mutation in the beta chain where a glutamic acid (polar) residue is substituted for a valine (hydrophobic) at position 6 of the beta-chain (nonconservative substitution). Homozygous expression of HbS produces sickle cell disease (~50 % sickled cells) where the sickled cells are more fragile and have shorter half-lives causing chronic hemolytic anemia as well as a vaso-occlusive condition (may be fatal). Also, these sickle/crescent shaped cells get trapped in small blood vessels leading to tissue damage causing various conditions leading to a reduced-life span. Heterozygotes are usually asymptomatic (~1% sickled cells) and are protected against the lethal form of malaria.

Hemoglobin C

HbC is found in people with hemoglobin C disease and is characterized by a mutation in the beta globin gene where glutamic acid at position 6 is substituted by lysine. Hemoglobin C disease is rare and relatively benign. HbC does not form tactoids, but intracellular blunt ended crystalloids resulting in decreased red blood cell survival time due to increased susceptibility to dehydration. The HbC trait is asymptomatic. If an HbC is inherited by both parents, it results in HbCC which causes microcytosis (abnormal small RBCs) and a mild form of hemolytic anemia.

Hemoglobin E

HbE contains a mutation in the hemoglobin beta chain where glutamate at position 26 is replaced by lysine resulting in mild hemolytic anemia, microcytic red blood cells, and mild splenomegaly. The heterozygous state is asymptomatic but causes microcytosis without anemia. The homozygous state has more severe microcytosis and hypochromia (abnormal decrease in the hemoglobin content), but only mild anemia.

Hemoglobin Constant Springs

HbCSpr is characterized by a mutation in the alpha globin gene that changes the mRNA stop codon and produces an alpha globin chain that is abnormally long (~30 amino acids longer). The quantity of hemoglobin in the cells is low because the mRNA for Hb Constant Spring is unstable and some is degraded prior to protein synthesis. In addition, the Constant Spring alpha chain protein is itself unstable. Homozygotes display mild hemolytic anemia and splenomegaly (enlarged spleen). The HbCSpr trait is asymptomatic.

Hemoglobin Barts

HbBarts is formed of four gamma chains when there is a shortage of alpha chains. Overall, they are not very soluble so that they accumulate in red blood cells. This variant develops in fetuses with four-gene deletion alpha thalassemia. During normal embryonic development, the epsilon gene of the alpha globin gene locus combines with genes from the beta globin locus to form functional hemoglobin molecules. The epsilon gene turns off at about 12 weeks, and normally the alpha gene takes over. With four-gene deletion alpha thalassemia no alpha chain is produced. The gamma chains produced during fetal development combine to form gamma chain tetramers. These molecules transport oxygen poorly. Most individuals with this Hb variant die in utero.

Hemoglobin H

HbH is a tetramer composed of four beta globin chains and only occurs with extreme lack of alpha chains. Although each of the beta globin chains is normal, HbH does not function normally. It has an increased affinity for oxygen which prevents it from releasing oxygen to the tissues and cells. HbH can result in fewer red blood cells with mild to moderate anemia but usually no clinical symptoms develop.

Hemoglobin SC

Patients with HbSC disease inherit a gene for hemoglobin S from one parent, and a gene for hemoglobin C from the other. HbC interacts with HbS producing some of the abnormalities seen in sickle cell patients. On average, clinical severity of this condition is milder than the one of sickle cell disease. However, some people with HbSC disease have a condition equal in severity to that of any patient with sickle cell disease. The HbS trait is usually asymptomatic, while the HbC trait only slightly disturbs the red cell metabolism.

Hemoglobin Gun Hill

This variant is rare and inherited in an autosomal dominant pattern causing chronic hemolytic anemia. It is characterized by a deletion of five amino acids in the β-chains which results in unstable hemoglobin due to impaired heme binding which results in half the expected number of heme groups. Also, Hb gun Hill is characterized by a high oxygen affinity (so that Hb less likely to release oxygen to body tissues) and a lack of the Bohr Effect.

Hemoglobin Lepore

HbLepore is characterized by an abnormal hybridization between two chains which results from a "crossover" between the delta and beta globin gene loci. Thus, it has two normal alpha chains and two delta beta fusion chains. Heterozygotes form about 10% Hb Lepore, normal amounts of Hb A2, and moderately increased amounts of Hb F and usually have mild anemia, microcytosis, and hypochromia. Homozygotes form only Hb Lepore and Hb F and have severe anemia, but are quite rare. There are three varieties of Hb Lepore named Boston, Baltimore and Hollandia which differ in the region of crossing over. The Hb Lepore trait is an asymptomatic condition.

Hemoglobin FTexas

HbFTexas is an abnormal fetal hemoglobin which is abnormally acetylated; a lysyl residue is substituted for either the fifth or sixth glutamyl residue of the gamma-chain.

References

http://sickle.bwh.harvard.edu/hemoglobinopathy.html

http://web2.airmail.net/uthman/hemoglobinopathy/hemoglobinopathy.html

http://bloodjournal.hematologylibrary.org/cgi/content/short/32/3/355

http://www.ahealthstudy.com/diseases/hemoglobin-c-s-c-d-e-disease

http://www.ncbi.nlm.nih.gov/pubmed/14259765