Hemoglobin C is an inherited variant of normal adult hemoglobin (hemoglobin A). It results from a substitution of lysine for glutamic acid in the sixth position of the beta (β) globin chain. The gene for Hemoglobin C has the highest frequency among people of African heritage (about 1 in 50). However, it is also found in people of Middle Eastern and Mediterranean (Italian, Greek, Turkish) descent. Summarized below are the four most commonly encountered hemoglobin patterns that involve hemoglobin C.

**Hemoglobin C Trait** (phenotype: FAC in infants and AC in adults)
Hemoglobin C trait results when the gene for hemoglobin C is inherited from one parent and the gene for hemoglobin A from the other. This carrier state does not usually result in health problems, although there may be a slightly low MCV and target cells. For an infant identified with hemoglobin C trait on two newborn screening specimens, no further testing is indicated for the child. However, it is strongly recommended that the parents have hemoglobin testing to determine if they may be at risk for having subsequent children with hemoglobin sickle C disease, a clinically significant form of sickle cell disease (described below), which is inherited in an autosomal recessive fashion.

**Homozygous Hemoglobin C or Hemoglobin C Disease** (phenotype: FCC in infants and CC in adults)
Homozygous hemoglobin C disease results when the gene for hemoglobin C is inherited from both parents. A mild hemolytic anemia develops in the first few months of life as the amount of fetal hemoglobin decreases and hemoglobin C increases. Individuals with homozygous hemoglobin C may develop splenomegaly and jaundice. Although uncommon, there can be sporadic episodes of musculoskeletal pain and aplastic crises. Also, pigmented gallstones may develop in adulthood.

**Hemoglobin Sickle C Disease** (phenotype: FSC in infants and SC in adults)
Compound heterozygotes with hemoglobin sickle C disease result when the gene for hemoglobin C is inherited from one parent and the gene for hemoglobin S (commonly known as sickle cell) from the other. A moderate hemolytic anemia develops in the first few months of life as the amount of fetal hemoglobin decreases and hemoglobin S and C increases. Infants and children with hemoglobin sickle C disease are particularly susceptible to bacterial infections and splenic sequestration, each of which can result in death. Prophylactic oral penicillin and folic acid should be started before three months of age and maintained through age six to decrease the morbidity associated with the disease. Some long-term manifestations of hemoglobin sickle C disease are recurrent pain episodes and tissue infarction with organ damage and failure. There is also a risk for splenomegaly, retinal disease and aseptic necrosis.

**Hemoglobin C/β Thalassemia** (phenotype: FCA or FC in infants and CA or C in adults)
Co-inheritance of the gene for hemoglobin C and β thalassemia, termed hemoglobin C/β thalassemia, has clinical manifestations ranging from mild to moderate, depending upon the degree of the thalassemia affecting the hemoglobin A gene. Individuals with hemoglobin C/β° thalassemia have a moderately severe disease marked by splenomegaly and occasional bone changes. Most individuals with hemoglobin C/β+ thalassemia have a mild anemia marked by a low MCV and target cells.

*Genetic counseling is advisable for families affected by these conditions to promote understanding of the significance for themselves and future offspring. A list of genetic counselors and hemoglobin consultants was included with this fact sheet (additional copies are available from our office).*