HEMOGLOBINOPATHIES

The hemoglobinopathies are a group of inherited disorders where there is abnormal production or structure of the hemoglobin molecule. Hemoglobinopathies represent the most common single cell recessive disorders worldwide.

There are two main types of hemoglobinopathies:

Thalassemia Syndromes

Disorders of decreased globin chain production

Alpha Thalassemia

Beta Thalassemia

Hemoglobin Variants

Disorders that produce structurally abnormal globin proteins

Hemoglobin S, C, E, etc.

A combination of the two is also possible.

Alpha Thalassemia

There are four copies of the alpha globin gene present in an unaffected individual, two on each chromosome 16 Clinical findings depend on the number of alpha globin genes deleted

Silent Carrier

- One alpha globin gene deleted
- Normal CBC & Hb Elect

Alpha Thalassemia Trait

- Two alpha globin gene deleted (CIS form = both genes deleted on the same chromosome; TRANS form = one gene deleted from each chromosome)
- Normal CBC & Hb Elect

Hemoglobin H Disease

- Three alpha globin gene deleted
- Hb H present on Hb elect
- Variable clinical presentation

Hemoglobin H-Constant Spring

- Two alpha globin gene deleted in CIS, plus a Constant Spring variant on a third alpha globin gene
- Hb H present on Hb elect
- More severe clinical course than Hemoglobin H disease
- Likely to require transfusions
- Moderate to severe splenomegaly, growth delay

Alpha Thalassemia Major

- All four alpha globin gene deleted
- Hb Barts present on Hb elect
- Survival is possible through intrauterine intervention. Following birth, regular transfusion therapy and chelation required.

Beta Thalassemia

There are two copies of the beta globin gene present in an unaffected individual, one on each chromosome 11. Beta plus variants cause decreased beta globin production, and beta null variants cause a complete absese of beta globin production. Clinical findings depend the type of beta globin variant(s) present.

Beta Thalassemia Trait

- One beta globin variant present (beta plus OR beta null)
- Mild anemia, low MCV on CBC
- Mildly elevated HbA2 on Hb Elect

Beta Thalassemia Intermedia

- Usually results from the presence of two beta plus variants
- Lesser clinical severity than thalassemia major
- Presentation includes moderate anemia, splenomegaly, moderate to severe hepatomegaly and bony changes
- Transfusions not usually required to survive, but rather to improve quality of life;
- Chelation therapy may be required

Beta Thalassemia Major

- Two beta globin variants present (either one beta plus and one beta null or two beta null variants)
- Severe anemia (fatal if untreated),
- Splenomegaly, growth delay
- Secondary iron overload causing organ damage if untreated
- Management includes chronic transfusions, chelation therapy and ongoing monitoring for complications

SICKLE CELL DISEASE

There are two copies of the beta globin gene present in an unaffected individual, one on each chromosome 11. Hemoglobin S results from a specific variant in the beta globin genes, causing red blood cells form a "sickle" shape when deoxygenated, resulting in clinical consequences.
The type of features will depend on when a person has one or two copies of hemoglobin S variant present, or if other beta globin variants are also present.

Sickle Cell Trait

- One hemoglobin S variant present
- Hemoglobin S seen on Hb Elect
- Minimal clinical issues with normal overall life expectancy

Hemoglobin C Trait

- One hemoglobin C variant present
- Slightly lower MCV
- Hemoglobin C seen on Hb Elect
- Clinically asymptomatic

Hemoglobin E Trait

- One hemoglobin E variant present
- Low MCV with microcytosis
- Hemoglobin C seen on Hb Elect
- Clinically asymptomatic

Sickle Cell Disease

- Two hemoglobin S variants present
- Onset in early childhood
- Moderate to severe hemolytic anemia
- Recurrent pain episodes **
- Increased incidence and severity of certain infections
- Tissue infarction leading to organ damage and failure
- Management includes:
  - Accurate, early diagnosis
  - Education / prompt recognition of complications
  - Prevention / treatment of infections
  - Management / aggressive treatment of acute vaso-occlusive events, chronic pain and hemolytic anemia
  - Screening for early signs of organ damage
  - Therapeutic intervention

Hemoglobin SC Disease

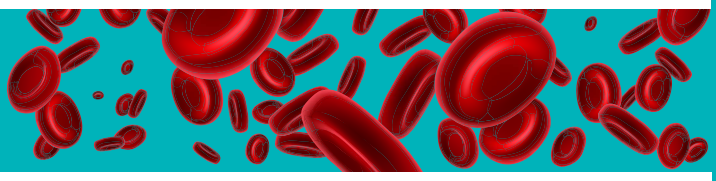
- Two beta globin gene variants present - hemoglobin S and hemoglobin C
- Usually milder than sickle cell disease
- Mild hemolytic anemia
- Occasional infarctive crises
- Splenomegaly
- Increased viscosity of the blood

Hemoglobin S-Beta Thalassemia

- One hemoglobin S variant AND one beta thalassemia variant present
- Moderate to severe hemolytic anemia
- Recurrent pain episodes
- Splenomegaly
- Clinical severity depends on the type of beta thalassemia variant inherited
  - Hemoglobin S-beta plus thalassemia tends to be less severe than Hemoglobin S-beta null thalassemia
  - Often difficult to distinguish between sickle cell disease and Hemoglobin S-beta null thalassemia on Hb elect

Hemoglobin E Sickle Cell

- One hemoglobin E variant AND one hemoglobin S variant present
- Mild to moderate hemolytic anemia
- Clinical expression is variable: some patients have no symptoms, whereas others have sickle cell-related complications.
- Less severe as compared to more common forms of sickle cell disease.



For more information about about local resources for these conditions, scan the QR code or visit our website

nymacgenetics.org/us-virgin-islands

NYMAC regional genetics network

These resources are supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $861,180 with 0 percent financed with non-governmental sources. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit HRSA.gov.