Overview

Beta-thalassemia is an inherited blood disorder that can cause mild to severe anemia (a decrease in the production of healthy blood cells) in children or adults. Beta-thalassemia occurs due to changes in the genetic code of the *HBB* gene. The *HBB* gene is responsible for producing the beta subunit of the hemoglobin protein. Genetic changes in *HBB* that cause beta-thalassemia result in red blood cells being ineffective at transporting oxygen in the body. Genetic changes causing beta-thalassemia may be passed from parent to child. Screening measures are available to identify individuals at risk for beta-thalassemia. There are 3 subtypes of beta thalassemia: beta-thalassemia minor, beta-thalassemia intermedia, and beta-thalassemia major. Each subtype is named based on the degree of anemia severity.

Symptoms

1) **Beta-thalassemia minor:** Individuals with beta-thalassemia minor typically show only mild symptoms of anemia and usually do not need any medical treatment.
2) **Beta-thalassemia intermedia:** Individuals with beta-thalassemia intermedia show moderate to severe symptoms of anemia and require less frequent medical treatment compared to individuals with beta-thalassemia major. Symptoms of beta-thalassemia intermedia and beta-thalassemia major are very similar and emerge between 6 months and 2 years of age. (see section below).
3) **Beta-thalassemia major (also known as Cooley's anemia or Mediterranean anemia):** Individuals with beta-thalassemia major show severe symptoms of anemia and require consistent medical treatment.
    a) **Presenting symptoms observed in most children:**
        - Pale skin (pallor)
        - Yellow skin (jaundice)
        - Slow growth and development (failure to thrive)
        - Poor appetite
        - Diarrhea
        - Enlarged belly
    b) **Possible later onset symptoms:**
        - Heart complications
        - Liver complications
        - Hormone complications

Treatment

The most common treatments for beta-thalassemia intermedia and beta-thalassemia major are blood transfusions and iron chelation therapy. There are additional therapies currently under study for treatment, especially for individuals with beta-thalassemia major.

1) **Blood transfusions:** The procedure ranges from 1 to 4 hours. Affected individuals receive donated blood which restores the number of red blood cells in the body. While individuals with beta-thalassemia major require frequent blood transfusions, individuals with beta-thalassemia intermedia may only require occasional blood transfusions in the event of illness or before undergoing surgery.
2) **Iron chelation therapy (medication):** Iron overload may occur in individuals with beta-thalassemia intermedia and beta-thalassemia major as a result of blood transfusions. Iron buildup is toxic to the body and the body is unable to naturally rid itself of iron. Medications called iron chelators bind to iron in order to prevent damage to healthy tissues.
3) **Investigational therapies:** These additional therapies include stem cell transplants, gene therapy, and certain medications. If interested in learning more, please visit https://www.clinicaltrials.gov.

Diagnosis

Your physician or genetic counselor is able to discuss the screening measures listed below with you.

Parental screening measures: The estimated risk that each parent has to pass down beta-thalassemia (risk to be carriers) to their children can be assessed in 2 ways. Complete blood count (CBC) and Hemoglobin electrophoresis are both blood tests that examine properties of the hemoglobin protein.

Baby screening measures: If both parents are identified as carriers, further tests may be performed in the baby.

a) **Chorionic villus sampling (CVS):** A small tissue sample from the placenta is tested around the 11th week of the pregnancy.

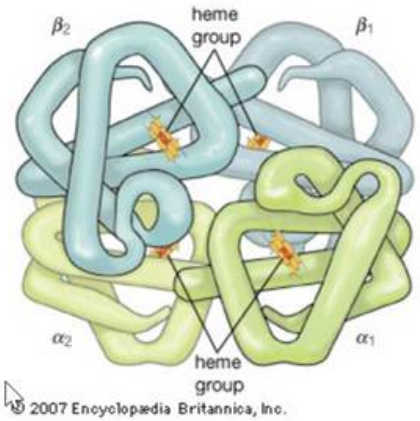
b) **Amniocentesis:** Fluid surrounding the baby called amniotic fluid is extracted for testing between the 15th to 20th week of pregnancy.

Management

- Regular blood tests and physicals
- Psychosocial support
- Avoidance of iron containing therapies to prevent risk of iron overload

Common Populations

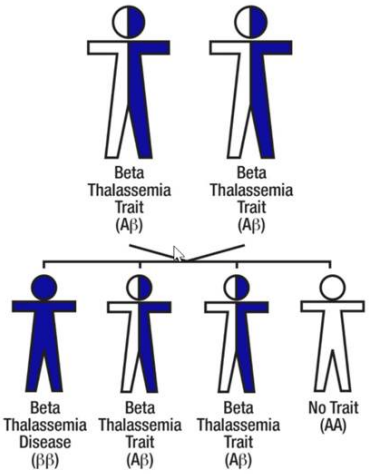
Beta-thalassemia is most prevalent in regions where malaria is common such as the Mediterranean, Sub-Sharan Africa, the Middle East, and Southeast and Central Asia. Individuals with these ancestral backgrounds are at increased risk to be carriers of beta-thalassemia.



Inheritance

The beta-globin gene (*HBB*) makes a protein called hemoglobin. Hemoglobin is found in red blood cells and carries oxygen throughout the body. Individuals with beta-thalassemia have either 1 or 2 mutations in the *HBB* gene.

1) **Beta-thalassemia minor (carrier):** Individuals with beta-thalassemia minor have 1 mutation in the *HBB* gene passed down to them from one of their parents. Having only 1 working copy of the gene is known as being a carrier. The *HBB* gene of these individuals is able to produce a working hemoglobin protein. If both parents have beta-thalassemia minor, there is a 25% chance to have a child with either beta-thalassemia intermedia or beta-thalassemia major.



2) **Beta-thalassemia intermedia and beta-thalassemia major:** Individuals with beta-thalassemia intermedia and beta-thalassemia major have gene changes in both copies of their *HBB* gene, with 1 *HBB* mutation (gene change) inherited from each parent. However, individuals with beta-thalassemia intermedia are able to produce some working protein while those with beta-thalassemia major produce no working protein.

3) **Risks for other Hemoglobinopathies:** Individuals may inherit 1 HBB mutation as well as a mutation of another blood disorder such as sickle cell anemia. The interaction between these 2 mutations may produce similar clinical findings such as anemia.

Resources

1) **Patient resources**

https://www.hopkinsmedicine.org/health/conditions-and-diseases/beta-thalassemia
https://rarediseases.org/rare-diseases/thalassemia-major/
https://www.clinicaltrials.gov
https://www.my46.org/learning-center/traits?search=thalassemia&submit=Search
https://www.kidshealth.org/en/parents/beta-thalassemia.html
https://www.thalassemia.org

2) **Medical resources**

https://www.ncbi.nlm.nih.gov/books/NBK531481/
https://www.nature.com/articles/gim201012

3) **Picture resources**

https://www.medicalnewstoday.com/articles/321530