# Understanding Thalassemia: What's not cool about Cooley's anemia

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## WHAT IS "THALASSEMIA"?

Thalassemia is an inherited condition involving a decrease in the components of hemoglobin. Hemoglobin is the protein in red blood cells that carries oxygen to the body. If the hemoglobin level is too low your child may experience pallor, low energy and poor growth.

The term thalassemia comes from the Greek word *thalassa* meaning "sea". It was initially felt to be a disease of the Mediterranean population, but we now know that it is also found throughout Africa, India and South East Asia as well. The more severe forms of beta thalassemia (Cooley's anemia) are seen typically in people of Mediterranean background, whereas severe alpha thalassemia (Hemoglobin H or hydrops fetalis) is usually seen in people from South East Asia.

***Figure 1.***
***Light areas indicate regions at increased risk for thalassemia.***

## HOW DO I KNOW IF MY CHILD HAS THALASSEMIA?

A blood test that will accurately screen for thalassemia is available at all medical laboratories.

A complete blood count will identify if there is any anemia (low hemoglobin) or if the size of the red blood cells is small.

If the child is anemic or the red blood cells are small, the next step is to sort out whether this is from thalassemia or iron deficiency (decrease of iron in the blood), a very common problem in children. A ferritin level is very helpful as is it will tell the doctor if the child has adequate iron stores. A low ferritin would support the diagnosis of iron deficiency while a normal level would suggest thalassemia.

## HOW WILL THALASSEMIA AFFECT MY CHILD?

The diagnosis of thalassemia in a child can mean anything from only having to test their future partner before having children (hopefully a long way off) to a severe life threatening illness. Fortunately, the severe forms are far less common than the minor forms of thalassemia.

**IS THERE ONLY ONE KIND OF THALESSEMIA?**

No, there are a variety of types. Thalassemia can vary from:

- **Silent** - no laboratory (blood work) or clinical changes (physical changes/symptoms)
- **Minor (or trait) -** only laboratory changes
- **Intermedia (Hemoglobin H)** - laboratory and variable clinical changes
- **Major** - severe illness requiring lifelong transfusions
- **Hydrops fetalis -** incompatible with life

**All figures in this text have been adapted from www.thalassemia.com*

*All of the various types of thalassemia will be detected by a complete blood count except for the silent carriers (only one of the four alpha globin genes is not working). The only time it is necessary to diagnose a silent carrier would be if that person were planning on having a child with a person known to have thalassemia.*

Thalassemia is divided into two groups: alpha and beta depending on which component of hemoglobin is affected.

Most adult hemoglobin is made up of two beta globin chains and two alpha globin chains. The various clinical presentations (physical complaints) of thalassemia we see are dependent on two factors: (1) which production genes are affected, and (2) the number of genes affected.

***Beta globin*** is made on the eleventh chromosome (or gene) and is fairly straightforward - one gene comes from the child's father and the other from the child's mother. Therefore a child with beta thalassemia can have either one (**minor** or trait) or both (**major**) of the genes affected.

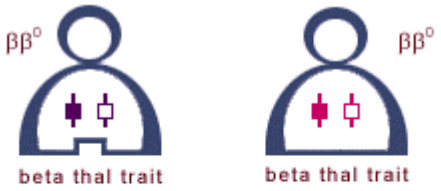
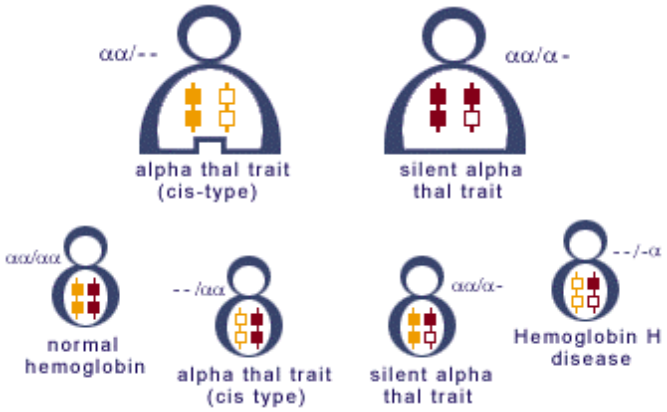



***Figure 2**. Beta globin depiction of parents each with one defective gene (darkened symbol), and one normal gene(lightened symbol). Offspring will result in one of the four scenarios shown.*


Alpha globin is made on the sixteenth chromosome and is more complicated. Because alpha globin is so essential to life we have evolved so that there are two genes which make the same thing. This means that a child will get two genes from each parent resulting in four possible scenarios: one (**silent**), two (**minor**), three (**Hemoglobin H**) or four (**hydrops fetalis**) genes can be missing.



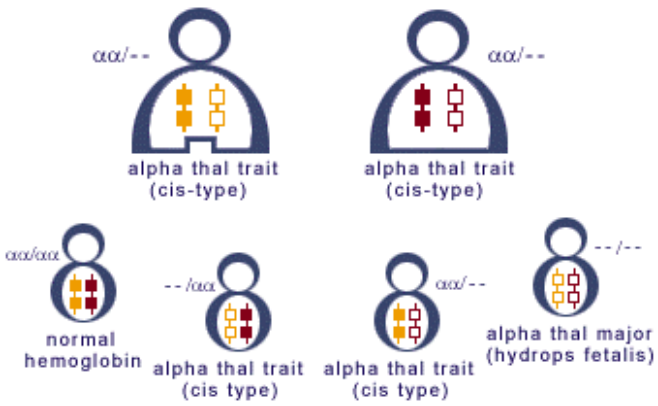




***Figure 3 (left).** Alpha globin depiction of parent, one with two genes defective and the other with one defective gene (darkened symbol: normal gene; lightened symbol: defective gene). Offspring will result in one of the four scenarios shown.*

***Figure 4 (right).** Alpha globin depiction of parents both with two defective genes. Offspring will result in one of the four scenarios shown.*

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## SO WHAT TYPE DOES MY CHILD HAVE?

A definitive diagnosis of thalassemia is difficult.

Beta thalassemia can be readily diagnosed by doing an additional blood test called a hemoglobin electrophoresis. The electrophoresis test will quantify the different types of hemoglobin in the blood.

*Many physicians mistakenly think that a normal electrophoresis "rules out" thalassemia, but in the alpha type of thalassemia this test will be normal.*

The diagnosis of alpha thalassemia tends to be more a diagnosis of exclusion i.e. the red cells are small and the ferritin level is normal or there is no response to iron supplementation. A parent with the same blood picture would confirm an alpha thalassemia diagnosis.

Genetic testing is the gold standard but is not readily available to most physicians and usually requires referral to a hematologist.

## WHAT IS MY CHILD'S DIAGNOSIS?

Depending on the type of thalassemia your child has, he/she will be diagnosed as having one of the following thalassemias:

### Thalassemia Minor

Thalassemia minor includes children who have a problem with only one of the their two beta globin genes or only two of their four alpha globin genes. These children are often picked up on routine childhood blood testing and initially may be diagnosed as being iron deficient. The diagnosis of thalassemia minor occurs when there is a lack of response to iron therapy, lack of good iron stores, and an ethnic origin that is at increased risk for thalassemia.

#### How do we treat Thalassemia minor?

Thalassemia minor is of no clinical consequence and no therapy is necessary. When the child reaches the age where he/she is planning a family, it is important to know the status of the partner to avoid having an offspring with severe thalassemia. It is also good to know so that the child is not misdiagnosed as being iron deficient.

### Thalassemia Major

Thalassemia major, also known as Cooley's anemia, occurs only in children who have abnormal function of both of their beta globin genes.

Thalassemia major usually presents in the first year of life with poor feeding and growth, pallor, low energy and frequent infections. There may also be bone deformities and enlargement of the liver and spleen. Diagnosis is by hemoglobin electrophoresis.

#### How do we treat Thalassemia Major?

Treatment of this disorder involves life long blood transfusions, typically every 4 weeks. Because of the frequency of these transfusions the child is at risk for blood-borne infections, resistance to transfusions and most importantly iron overload. Special care must be taken to manage the iron loading of these patients otherwise they will not live past their twenties due to heart failure from iron buildup in the heart. The good news is that there is an effective medication that helps eliminate the iron and with this therapy, children with thalassemia major can live an almost normal life span. Unfortunately, presently

the medication must be injected under the skin as a ten-hour infusion every night for their whole life. Hopefully an oral form of this medication will soon become available to improve the quality of life of these children.

**Do we have any other options other than blood transfusion?**

Bone marrow transplantation is generally recommended for children who have a genetically matched brother or sister. The risks of an unrelated donor transplant disqualify bone marrow transplantation in patients who don't have a matched sibling.

## Thalassemia Intermedia

Children who have three of their four alpha genes affected have thalassemia intermedia also called hemoglobin H disease.

**How do we treat Thalassemia Intermedia?**

The clinical course for this group of patients is quite variable with some patients needing regular transfusions and others never requiring a transfusion. The decision to start transfusion is a difficult one that depends on many factors including growth, level of hemoglobin, bone disease and pubertal development.

**Hydrops Fetalis**

Fetuses who have loss of function of all four of their alpha globin genes develop a very serious condition called hydrops fetalis and are stillborn.

**How can you prevent Hydrops Fetalis?**

Genetic counseling for couples who have thalassemia minor (in particular those originating from South East Asia) may help avoid this deadly form of thalassemia.

***FINAL THOUGHTS…..***

Thalassemia can be a puzzling diagnosis. Fortunately, the majority of children show no symptoms and require no treatment. With proper diagnosis and counseling, the specific type of thalassemia can be identified and the appropriate course of action (or inaction) can be prescribed.

***A child with thalassemia CAN live an active and normal life… Contact your family physician for more information.***