



Thalassaemia



Adult hemoglobin (HbA) contains two alpha chains and two beta chains. In thalassaemia, there is deficient synthesis of either the alpha chains or the beta chains. Symptoms are a result of not only low levels of HbA, but also the relatively high levels of the chain that is synthesized.

Thalassaemia is an inherited disease of faulty synthesis of hemoglobin. The name is derived from the Greek word "thalassa" meaning "the sea" because the condition was first described in populations living near the Mediterranean Sea; however, the disease is also prevalent in Africa, the Middle East, and Asia.

Thalassaemia consists of a group of disorders that may range from a barely detectable abnormality of blood, to severe or fatal anemia. Adult hemoglobin is composed of two alpha (α) and two beta (β) polypeptide chains. There are two copies of the hemoglobin alpha gene (*HBA1* and *HBA2*), which each encode an α -chain, and both genes are located on chromosome 16. The hemoglobin beta gene (*HBB*) encodes the β -chain and is located on chromosome 11.

In α -thalassaemia, there is deficient synthesis of α -chains. The resulting excess of β -chains bind oxygen poorly, leading to a low concentration of oxygen in tissues (hypoxemia). Similarly, in β -thalassaemia there is a lack of β -chains. However, the excess α -chains can form insoluble aggregates inside red blood cells. These aggregates cause the death of red blood cells and their precursors, causing a very severe anemia. The spleen becomes enlarged as it removes damaged red blood cells from the circulation.

Deletions of *HBA1* and/or *HBA2* tend to underlie most cases of α -thalassaemia. The severity of symptoms depends on how many of these genes are lost. Loss of one or two genes is usually asymptomatic, whereas deletion of all four genes is fatal to the unborn child.

In contrast, over 100 types of mutations affect *HBB*, and deletion mutations are rare. Splice mutations and mutations that occur in the *HBB* gene promoter region tend to cause a reduction, rather than a complete absence, of β -globin chains and so result in milder disease. Nonsense mutations and frameshift mutations tend to not produce any β -globin chains leading to severe disease.

Currently, severe thalassemia is treated by blood transfusions, and a minority of patients are cured by bone marrow transplantation. Mouse models are proving to be useful in assessing the potential of gene therapy.

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