The term Thalassemia is derived from the Greek word "Thalassa" meaning "the sea" as the patients were initially identified in the Mediterranean area. It is also termed as "Mediterranean Anaemia". It was first identified by Cooley & Lee in 1925, hence also named as Cooley's Anaemia.

Thalassemia is an inherited blood disorder in which the body is unable to make adequate haemoglobin. Haemoglobin is present in the red cells. Normally red cells survive for 120 days but in Thalassemia red cell survival is reduced.

According to joint WHO-March of Dimes report 2006, approximately 7% of the global population is a carrier for Haemoglobin disorders with no health problems. Around 300,000 – 500,000 children are born annually with a severe haemoglobin disorder. Over 1,00,000 Thalassemia Major are born annually world over. Throughout the world there is a "Thalassemia Belt" that includes from countries around Mediterranean Sea like Italy, Greece, Cyprus, Sardinia and passes through West and Central Asian countries like Turkey, Saudi Arabia, Iran, Afghanistan onto Pakistan, India and South East Asian countries like Burma, Thailand & Indonesia,. Migrants/Descendants from these areas to other parts of world are also at high risk of carrying BTT.

What is Thalassaemia ?

Introduction

Thalassaemia may have originated over 50,000 years ago in a valley south of Italy and Greece now covered by the Mediterranean Sea. The name Thalassaemia is derived from a Greek word meaning sea. But Thalassemia was recognized as a clinical entity by Dr Thomas Cooley and Dr Pearl Lee who described five cases of Thalassaemia in 1925.

The thalassemias are a diverse group of genetic blood diseases characterized by absent or decreased production of normal hemoglobin, resulting in a microcytic anemia of varying degree. Thalassemia includes a number of different forms of anemia (red blood cell deficiency). The two main types are called alpha and beta thalassemias, depending on which part of an oxygen-carrying protein (called hemoglobin) is lacking in the red blood cells.

The alpha thalassemias are concentrated in Southeast Asia, Malaysia, and southern China. The beta thalassemias are seen primarily in the areas surrounding Mediterranean Sea, Africa and Southeast Asia. Due to global migration patterns, there has been an increase in the incidence of thalassemia in North America, primarily due to immigration from Southeast Asia.

Alpha Thalassaemia

The alpha thalassemias are caused by a decrease in production of alpha globin chains due to a deletion or mutation of one or more of the four alpha globin genes located on chromosome 16. The alpha thalassemias can be generally categorized as: Silent Carrier,

Alpha Thalassemia Trait, Hemoglobin H disease, Hemoglobin H-Constant Spring, and Alpha Thalassemia major. Frequently, the diagnosis of alpha thalassemia trait in a parent is discovered after the birth of an affected child.

The most severe form of alpha thalassemia, results in fetal or newborn death. Most individuals with alpha thalassemia have milder forms of the disease, with varying degrees of anemia.

Beta thalassemia

Beta thalassemia, ranges from very severe to having no effect on health. There are three kinds of beta thalassaemia.

Thalassemia major, the most severe form, is also called Cooley's anemia, named after the doctor who first described it in 1925.

Thalassemia intermedia is a mild variety of Cooley's anemia.

Thalassemia minor (also called thalassemia trait) are symptomless, but changes in the blood do occur.

Causes
General

Thalassemia is an inherited condition. The disease is passed on through parents who carry the thalassemia gene in their cells. A "carrier" has one normal gene and one thalassemia gene also called as "thalassemia trait." Most carriers lead completely normal, healthy lives.

When two carriers become parents, there is a one-in-four chance that any child they have will inherit a thalassemia gene from each parent and have a severe form of the disease. There is a two-in-four chance that the child will inherit one of each kind of gene and become a carrier like its parents; and a one-in-four chance that the child will inherit two normal genes from its parents and be completely free of the disease or carrier state. These odds are the same for each pregnancy when both parents are carriers. The clinical severity of thalassemia varies tremendously depending on the exact nature of the genes that a person inherits.

Blood is made up of plasma (fluid), red blood cells, white blood cells and platelets. The white cells protect your body and fight against infections and the platelets are responsible for normal blood clotting. The red blood cells carry red blood protein called haemoglobin. Haemoglobin contains iron and transports oxygen from your lungs around the body. Anaemia is caused by reduced haemoglobin. If the anaemia is mild it does no harm and may not be noticeable.

A normal haemoglobin molecule contains four protein (globin) chains (two alpha globin chains and two beta globin chains) Different genes are responsible for producing each chain. In thalassaemia there is an inherited defect in one of these genes. If the alpha chain is affected this causes alpha thalassaemia. If the beta chain is affected this causes beta thalassaemia.

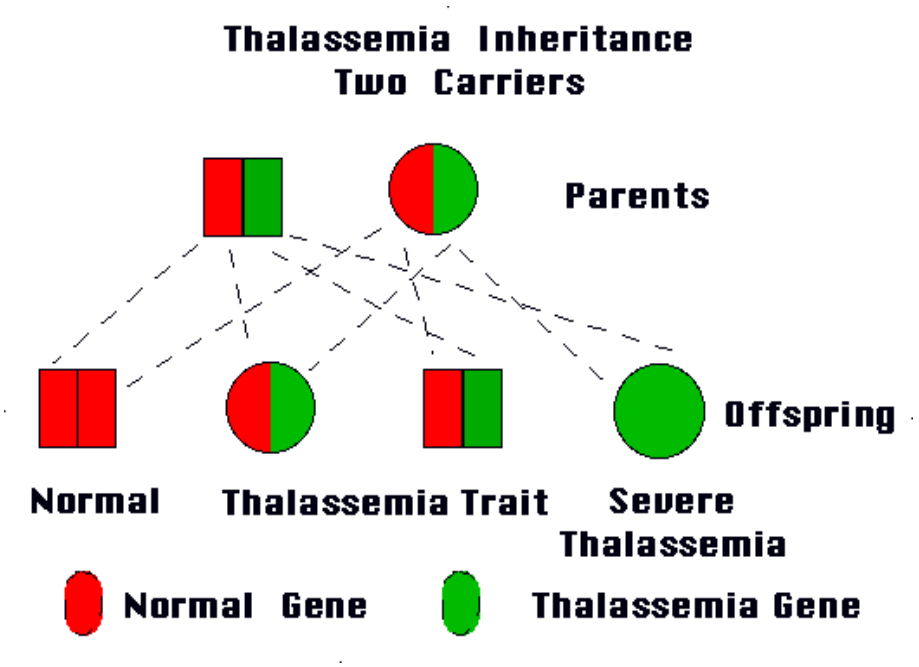
Causes of alpha thalassaemia

In alpha thalassaemia there is a decrease in the production of alpha globin chains due to a deletion (missing) or mutation (abnormal change) of one or more of the four alpha globin genes located on chromosome 16.

Causes of beta thalassaemia

Beta thalassemias are caused by mutations on chromosome 11.

When two carriers become parents, there is a one-in-four chance that any child they have will inherit a thalassemia gene from each parent and have a severe form of the disease. There is a two-in-four chance that the child will inherit one of each kind of gene and become a carrier like its parents; and a one-in-four chance that the child will inherit two normal genes from its parents and be completely free of the disease or carrier state. These odds are the same for each pregnancy when both parents are carriers.



Symptoms
Alpha Thalassaemia
Alpha plus Thalassaemia

This is very common in some ethnic groups. There are no symptoms and it usually goes unnoticed. There may be slight iron deficiency (anaemia) if the blood is tested for some reason. Sometimes people may be mistakenly diagnosed as having iron deficiency anaemia and be treated with iron medications unnecessarily.

Alpha Zero Thalassaemia

There are no symptoms and you are perfectly healthy. However if both parents have alpha zero thalassaemia they have a 1 in 4 chance of having a baby who has alpha zero thalassaemia major which is incompatible with life; the baby is often born prematurely and is dead or dies shortly after birth.

Beta Thalassaemia
Beta Thalassaemia Trait (Carrier)

There are usually no symptoms and you are perfectly healthy, however there are an increased number of cells and they are smaller than those without the condition. It can cause mild anaemia because slightly less haemoglobin is produced than normal. This usually does not cause you any symptoms and cannot be treated by increased iron intake.

Beta Thalassaemia major

Between births and three to six months, the baby with Beta thalassaemia major will seem normal and quite healthy. The baby will then begin to show symptoms of anaemia (they become pale) there may be shortness of breath, jaundice and an enlarged spleen.

Without treatment your child's bones will grow abnormally and death will occur early in childhood. Also if the condition is poorly treated or between transfusions your child will be pale, lethargic and breathless. There may be yellowing (jaundice) of the eyes and skin due to excessive breakdown of red blood cells. Also with poor treatment growth may be delayed, there may be osteoporosis of the bones and the spleen may be damaged.

Beta Thalassemia intermedia

Children with thalassemia intermedia may develop some of the same complications, although in most cases, the course of the disease is mild for the first two decades of life.

Treatment

Treatment for Beta thalassaemia major involves having regular blood transfusions, which take place every two to four weeks, depending on the severity of the anaemia. Excess iron builds up in the body from these regular transfusions. This is called iron overload. If

this is left untreated, iron will build up in the body, leading to a condition called haemosiderosis. This can cause serious long-term damage such as heart failure and liver failure.

Iron overload is kept under control by treatment with medicines Desferrioxamine, Deferiprone and/or Defrasirox to achieve a more normal level of iron in the body. These medicines work by binding (the chemical term is “chelating”) with the iron in the blood and the chelated iron is then removed through urine & stool from the body. Desferrioxamine has to be given by injection, usually by a slow injection under the skin via a small device or pump over eight to twelve hours. The Patient is taught how to do this at home. The amount of desferrioxamine and how often it is given depends on the how much iron you have in your body i.e. the amount of iron overload.

As you will be receiving this medicine regularly (often daily), it becomes tiresome for you and your family. So, it is important to understand why chelation doses should not be missed. Sticking to chelation treatment routines helps protect against serious complications in later life, such as diabetes and heart disease. There are also more immediate benefits such as prevention of nausea and sickness caused by iron overload.

Deferiprone is another medicine used to treat iron overload. It works in a similar way to desferrioxamine but is given by mouth. This medicine is only given to patients in whom desferrioxamine is not suitable or is not tolerated.

Defrasirox is relatively a newer oral iron chelator. It needs to be given just once a day as it works in the body for 24 hours. It has fewer side effects so drug of choice for iron chelation

Like all other medicines, Desferrioxamine, Deferiprone and Defrasirox too have side effects. You should refer to the manufacturer’s patient information leaflet for further information as well as talk to your doctor or pharmacist if you have any particular concerns. If you are receiving either of these medicines you need to be closely monitored by having regular blood tests (CBC SGOT, SGPT, Urea and Creatinine) once a month, Ferritin once in three months and eye and ear examinations annually. Liver, spleen size, body weight and height every three months be carried out in children because their growth can be affected by the condition and, in some cases, by the medicines.

Beta thalassaemia intermedia treatment may be the same as for Beta thalassemia major but as the anaemia is less severe, the need for transfusions or the frequency of transfusions and need for iron overload treatment will be different according to the severity of the anaemia.

Supplementary treatment

The time taken for iron to be removed from your body by desferrioxamine is improved by taking a daily dose of ascorbic acid (vitamin C). This is prescribed by your doctor according to your age and is usually started two weeks after starting desferrioxamine

treatment. If you have heart problems, you will not be given ascorbic acid because its combined effect with the iron in the blood may make the heart problem worse. Any other multivitamin and mineral supplements should not be taken unless prescribed. Calcium and vitamin D supplements are usually required.

Iron in the diet should be low- pomegranate, beetroot, jaggery, red meat, leafy vegetables etc. should be avoided. Tea along with meals reduces iron absorption from gut and vitamin C rich food should be avoided with meals because it increases the absorption of iron in food.

Other Treatments

Splenectomy – In thalassemia intermedia and under transfused thalassemia major patients' invariably spleen enlarges. Normal function of the spleen is to scavenge old and abnormal blood cells. When spleen is enlarged it starts removing both normal and abnormal blood cells precipitating into increased blood requirement, leucopenia (reduced white cells), thrombocytopenia (reduced platelets) and also discomfort in the abdomen. When spleen is slightly enlarged and blood cells are not reduced frequent transfusions may bring the size back to normal but if size is very big or there is continuous reduction in white cells or platelets splenectomy (removal of spleen by surgery) is the only solution. At least two weeks before the operation HiB, Meningococcal and pneumonia vaccination must be given and post-surgery life-long prophylactic penicillin is advisable.

Bone marrow transplantation – this can provide a cure for Beta thalassaemia major. Bone marrow is transplanted from a matched unaffected sibling or unrelated donor. It is best done when the child is very young. However, the procedure is costly and risky, although success rates are improving, they are unpredictable.

There are many emotional, psychological and social effects for the person with thalassaemia and their family, particularly as self- management is so important. Psychological support is important in managing chelation therapy and other aspects of the condition. You should get involved with local support groups and voluntary organizations for your own support and to help others.

FAQ's

1) How many types of Thalassaemia?
There are over 200 types of mutation causing Thalassaemia but clinically we can divide into two main types.
Thalassaemia Major
Thalassaemia Minor (Trait/Carrier)

2) What is Thalassaemia Major?
Thalassaemia major is also known as Cooley's Anaemia, Homozygous Bêta Thalassaemia or Mediterranean Anaemia. It is serious inherited blood disorder. Children

with Thalassaemia major cannot make enough haemoglobin. Their bone marrow cannot produce enough red blood cells. The red blood cells that are produced are nearly empty.

3) What is Thalassaemia Minor?
People with Thalassaemia Minor, sometimes known as Trait, carry Thalassaemia but they are not ill. They are completely healthy and normal, some of them have slight anaemia. Most people with Thalassaemia Minor do not even know that they have it. It is only discovered if the person has a special blood test or if they have a child with Thalassaemia Major. It is important to know if you have Thalassaemia Minor because if your partner is also thalassemia trait then your children may have Thalassemia major.

4) Who are Carriers of Thalassaemia and how many people are carriers of Thalassaemia around the World?

4.5% of world population is thalassemia trait and over 100,000 children born in the world with Thalassaemia major.

5) Who is likely to carry Thalassaemia?
People who are likely to carry the gene of Thalassaemia are people who are inhabitants of descendants from Mediterranean countries, Middle East, Indian subcontinent and South East Asian countries.

6) What are known cause for Thalassemia?
There is not a known cause for Thalassaemia except that is inherited through the genes.

7) What is the "quality of life" for a Thalassemic?
Thalassemia minors live absolutely normal life. Though Thalassemia major persons have some limitations in quality of life, especially when they don’t get adequate treatment. The treatment should not interfere with a Thalassemics life. In particular doctors and hospitals should make the effort to arrange patient’s visits to interfere as little as possible with normal life. Treatment should not interrupt schooling or work.

8) How long can a person with Thalassemia major live?
These days most Thalassemics are living a normal life and earn their own living. Most also find a partner and get married. Now a number of Thalassaemia major patients have their own children. Today it is reasonable to think that people with Thalassaemia major, who have been well treated from the beginning, may well live as long as people without Thalassaemia.

9) Can people with Thalassaemia major and minor have healthy children?
People with Thalassaemia major can have babies only if their partner does not carry any sort of Thalassemia. If a Thalassaemia major’s partner does not carry any Thalassaemia gene none of the children would have Thalassaemia major. But all their children will carry Thalassaemia minor.

10) Do Thalassaemia person need to be on a special diet?
Thalassaemia major patents should try to keep away from food rich in iron such as red meat, liver, kidney, green leafy vegetables such as spinach, Jaggery, breakfast cereals fortified with iron and alcohol. Although this is recommended, absolute aversion is not necessary in well transfused and adequately chelated patients.

11) How is the treatment improving?
Newer forms of treatment are being evolved making the treatment more comfortable and safe. There is a lot of development on permanent front also. Unrelated bone marrow transplantation and gene therapy has become a reality. Gene therapy would correct the defected gene in Thalassaemia patients and then transferring normal gene into the patient’s own bone marrow.