

5405
WHO/HDP/EM/HB-AT/94.4
Original: ENGLISH
Dist.: GENERAL

EDUCATIONAL MATERIALS

ON

HAEMOGLOBINOPATHIES:

ALPHA THALASSAEMIA



WORLD HEALTH ORGANIZATION
HEREDITARY DISEASES PROGRAMME
1994

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C O N T E N T S

	<u>Page</u>
SECTION I:	
INFORMATION FOR PEOPLE WHO CARRY ALPHA THALASSEAMIA TRAIT	1-4
SECTION II:	
INFORMATION FOR PEOPLE WHO HAVE HAEMOGLOBIN H DISEASE	5-23

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IMPORTANT NOTE

This section is for people with alpha thalassaemia trait, or "probable alpha thalassaemia trait", in whom a definitive DNA diagnosis of alpha plus or alpha zero thalassaemia trait has not been made. It is designed to give general information to doctors, midwives and other health workers, as well as patients. It points out that alpha thalassaemia trait is important only in specific ethnic groups, and indicates when further investigation, such as testing a partner, is advisable, and when it is not advisable. It should be available to health workers counselling people who have been given a diagnosis of "probable alpha thalassaemia trait". It is intended:

- (a) to be handed to patients of South-East Asian, Cypriot, Greek or Turkish extraction by the doctor or midwife, who will also give verbal information based on the leaflet;
- (b) to be helpful in counselling people originating from Africa, the Caribbean, South-East Asia or the Indian sub-continent who have been told they carry alpha thalassaemia trait and require reassurance;
- (c) to guide health workers in how to use ethnic group in deciding whether or not to proceed with further investigation of microcytosis with a low or normal Hb A₂ value.

SECTION I:

INFORMATION FOR PEOPLE WHO CARRY ALPHA THALASSAEMIA TRAIT

List of Contents

	<u>Page</u>
1. Introduction	2
2. Alpha plus thalassaemia	2
3. Alpha zero thalassaemia	3
4. Is there anything else I should do now?	3
ANNEX 1: List of National Thalassaemia Centres	4

1. INTRODUCTION

Thalassaemia is common among people originating from Africa, Asia, the Mediterranean area or the Middle East. It is common in these regions because it helps to protect carriers against malaria. It is rare in Northern Europeans.

Thalassaemia is a characteristic of the blood. It is inherited, that is, it is passed on from parents to children, just like hair colour, eye colour or skin colour. It is passed on equally by men and women. It is not catching, and will not turn into an illness.

There are two forms of thalassaemia: alpha thalassaemia (α thalassaemia) and beta thalassaemia (β thalassaemia).

This section is for people who have had a blood test that suggests they carry **alpha thalassaemia**. People who carry alpha thalassaemia are said to have alpha thalassaemia trait. This is often written α thalassaemia trait.

Alpha thalassaemia trait does not cause any illness. Most people with alpha thalassaemia trait do not know they have it. They only discover it when they have a special blood test. Alpha thalassaemia trait will never affect your own health. However, it can cause confusion, and in some cases it could affect the health of your children.

There are two types of alpha thalassaemia trait: alpha plus thalassaemia trait which is harmless, and alpha zero thalassaemia trait, which may have more serious implications.

2. ALPHA PLUS THALASSAEMIA

If you, or one or both of your parents or grandparents, or in fact any of your ancestors originally came from:

Africa (this includes Afro Caribbeans, unless they have some Chinese ancestry)
Bangladesh
India
Pakistan

then your alpha thalassaemia trait is harmless for your children.

You have a form of alpha thalassaemia called **alpha plus thalassaemia**. This is the mildest form of thalassaemia. It will never affect your health. You may pass it on to some of your children, but it will not affect their health.

About 1 in 3 people originating from Africa or the Indian sub-continent carry alpha plus thalassaemia trait. In fact, it is normal for many people whose ancestors came from these areas to carry mild alpha thalassaemia. So you should not worry about it.

It is useful for you to know that you carry alpha plus thalassaemia trait, because otherwise, when you have a blood test, doctors may think that you carry a more serious form of thalassaemia. This could worry you unnecessarily. Your alpha thalassaemia could also be mistaken for iron deficiency. In your case, iron deficiency can be diagnosed only by measuring your serum iron or ferritin level.

3. ALPHA ZERO THALASSAEMIA

If you carry alpha thalassaemia trait and you or your parents or grandparents, or in fact any of your ancestors originally came from

The Mediterranean area: Cyprus
Greece
Turkey
Southern Italy

The Middle East

South-East Asia: China (this includes people of Chinese origin from, e.g.,
Hong Kong, Singapore, Malaysia, Indonesia)
Kampuchea
Thailand
The Philippines
Vietnam

or if you do not know where your ancestors came from, or you are a North European, you could carry alpha-zero (α^0) thalassaemia trait

Alpha-zero thalassaemia trait is uncommon. It does not cause any illness. However, it could be a problem for some of the children of people who carry it. If both parents carry alpha-zero thalassaemia trait, some of their babies could have a very severe anaemia. But if they know they both carry alpha zero thalassaemia trait they can avoid this risk.

So if you have alpha thalassaemia trait and you come from China or another part of South-East Asia, the Mediterranean area or the Middle East, it may be important for you to find out which type of alpha thalassaemia you carry.

If you do not yet have a partner, remember that your alpha thalassaemia will not do you any harm. You need not do anything about it now. Once you have a partner, take him or her for a blood test before you have children. If your partner does not have any type of thalassaemia, there is no risk for your children, and you have nothing to worry about. But if your partner's blood test result shows any unusual finding that might be associated with thalassaemia, you should see an expert in haemoglobin disorders for advice.

If you are not sure what type of alpha thalassaemia you carry, and you need to find out, go to see your doctor, and take this document with you.

Your doctor can arrange further information, and tests for you when necessary, through your local consultant haematologist, or at one of the expert centres listed overleaf.

4. IS THERE ANYTHING ELSE I SHOULD DO NOW ?

You inherited your alpha zero thalassaemia from your father or your mother, so your brothers and sisters, and other blood relatives, could also be carriers. Show them this leaflet, and advise them to ask for a blood test for alpha thalassaemia trait before they have children.

ANNEX 1

List of National Thalassaemia Centres

SECTION II:

INFORMATION FOR PEOPLE WHO HAVE HAEMOGLOBIN H DISEASE

List of Contents

	<u>Page</u>
1. What is haemoglobin H disease?	6
2. How did I inherit haemoglobin H disease?	8
3. Will I pass haemoglobin H disease on to my children?	10
4. Is there anything else I should do now?	14
ANNEX 1: Personal Medical Record for People who have Haemoglobin H Disease	15

IMPORTANT NOTE

This section is for people with haemoglobin H disease, who have discussed it fully with an expert in haemoglobin disorders, and have had the diagnosis confirmed by DNA tests.

Haemoglobin H disease is rather complicated to explain. If you have not already discussed it with an expert in haemoglobin disorders, you should arrange to do so.

There are different forms of haemoglobin H disease. This section is about the commonest form, which rarely causes ill-health. Rarer, more severe forms also exist. They are not described here.

This section explains what your haemoglobin H disease means for you, how you got it, and whether you can pass it on to your children. It should also help you to explain it to other members of your family.

1. WHAT IS HAEMOGLOBIN H DISEASE ?

Haemoglobin H disease is a type of anaemia. It is a form of *alpha thalassaemia*,¹ which is an inherited characteristic of the blood. "Inherited" means that it is passed on from parents to children, like eye colour, hair colour or skin colour. It is passed on equally by men or women. It is not catching, and will not turn into a serious illness. Haemoglobin H disease is often called "Hb H disease", for short.

To explain haemoglobin H disease, we must first talk about blood, and anaemia.

Blood is part of your body. It is pumped round by your heart, and circulates in the blood vessels that spread it through your whole body. Blood carries air and food to the tissues of the body, and picks up wastes to take away.

Blood is made up of a light yellow liquid, called plasma, and of three types of "cells". In fact, your whole body is made up of tiny building blocks called cells, far too small to see. In most tissues they are stuck together, but in the blood they float round freely in the plasma. There are 3 types of blood cells: red cells, white cells and platelets. There are many more red blood cells than white blood cells. Alpha thalassaemia affects the red blood cells.

Red blood cells are full of haemoglobin, which is red. This is why your blood is red. Haemoglobin picks up oxygen from the air in your lungs, and carries it round to your tissues, where it lets it go. To live, your tissues need to breath, so they need oxygen.

New red blood cells are being made all the time in your bone marrow. Normal red blood cells only live about 120 days. Then they are destroyed in your spleen.

● What is anaemia?

The word anaemia means a shortage of blood. People with anaemia have fewer red blood cells than normal, or have too little haemoglobin in their red blood cells. If the anaemia is mild, it does no harm and you may not even notice it: but if it is severe, you are ill, because your tissues don't have enough oxygen.

The commonest form of anaemia is "iron deficiency anaemia". This can happen if you do not have enough iron in your diet. It can be cured by taking iron medicine. Haemoglobin H disease is quite different from iron deficiency anaemia. It is an inherited anaemia. It cannot be cured by taking any medicines.

● How do you measure anaemia?

By measuring the amount of haemoglobin in your blood. Your Haemoglobin level is described as grams (g) of haemoglobin (Hb) per decilitre (1/10 of a litre) of blood. For example, your haemoglobin level may be 8 g/dl.

¹

There is another form of thalassaemia called beta thalassaemia. This is quite different from alpha thalassaemia. Separate educational materials on beta thalassaemia (document WHO/HDP/EM/BB.BT/94.5) are available from the Hereditary Diseases Programme, World Health Organization, CH-1211 Geneva 27, Switzerland.

The usual haemoglobin level for men is about 13-16 g/dl. For women and children it is about 11-14 g/dl.

Moderate anaemia means a haemoglobin level of about 8-11 g/dl.

Severe anaemia means a haemoglobin level of less than 8 g/dl.

People with haemoglobin H disease usually have a haemoglobin level between 8 and 10 grams/decilitre (8-10 g/dl). That is, they have a moderate anaemia.

● **Will haemoglobin H disease do me any harm?**

This level of anaemia rarely does people with haemoglobin H disease any harm. Most are as healthy as other people. They can grow up normally, work, find a partner and have a family, in the same way as other people. However, complications such as enlargement of the spleen or worsening of the anaemia can occur. Therefore you should see a specialist doctor once a year. Your haemoglobin level should also be measured at least once a year. You, yourself, should keep a lifelong record of your haemoglobin level and the size of your spleen. *You will find a record chart in Annex 1.*

● **Does haemoglobin H disease require any special treatment?**

Usually not. Very occasionally people with haemoglobin H disease can get more anaemic rather suddenly, for example, if they have an infection. Often the anaemia gets better again quite quickly on its own, but if it is severe they may need a blood transfusion.

Sometimes (rarely) the spleen becomes big and begins to destroy the red blood cells faster than it should. This makes the haemoglobin fall and stay at a lower level than before. That is, the person's anaemia becomes more severe. This may make them feel unwell and need blood transfusions. Usually, if the spleen is taken out, the person becomes as well as they were before it began to destroy the red cells.

● **Can haemoglobin H disease be confused with any other conditions?**

Yes, in particular it can be confused with iron deficiency. It is important that both you and your doctor know you have haemoglobin H disease. If you see a new doctor you should tell them you have haemoglobin H disease and show them this leaflet.

● **Will treatment with iron help my haemoglobin H disease?**

No. However, people with haemoglobin H disease can get iron deficient, like other people, and may then need iron. It can be difficult for doctors to diagnose iron deficiency anaemia in people with haemoglobin H disease. You would need a special blood test (serum ferritin or serum iron measurement) to find out whether you are iron deficient.

2. HOW DID I INHERIT HAEMOGLOBIN H DISEASE ?

To answer this question, we need to explain about alpha thalassaemia.

● What is alpha thalassaemia, and how is it inherited?

There are several types of alpha thalassaemia. It is important to distinguish between *people who carry* alpha thalassaemia, and *people who have anaemia* due to alpha thalassaemia.

● Carriers of alpha thalassaemia

A *carrier of alpha thalassaemia* is someone who has inherited alpha thalassaemia from only one of their parents. Carriers are perfectly healthy and usually have no idea that they carry alpha thalassaemia. They can only be identified by special blood tests. Carriers of alpha thalassaemia are also said to have *alpha thalassaemia trait*. Usually, both parents of a person with haemoglobin H disease have alpha thalassaemia trait.

There are two types of alpha thalassaemia trait:

- Alpha plus thalassaemia trait. This is very common, and is usually harmless.
- Alpha zero thalassaemia trait. This is less common. It can sometimes have more important implications, when parents pass it on to their children.

● Anaemia due to alpha thalassaemia

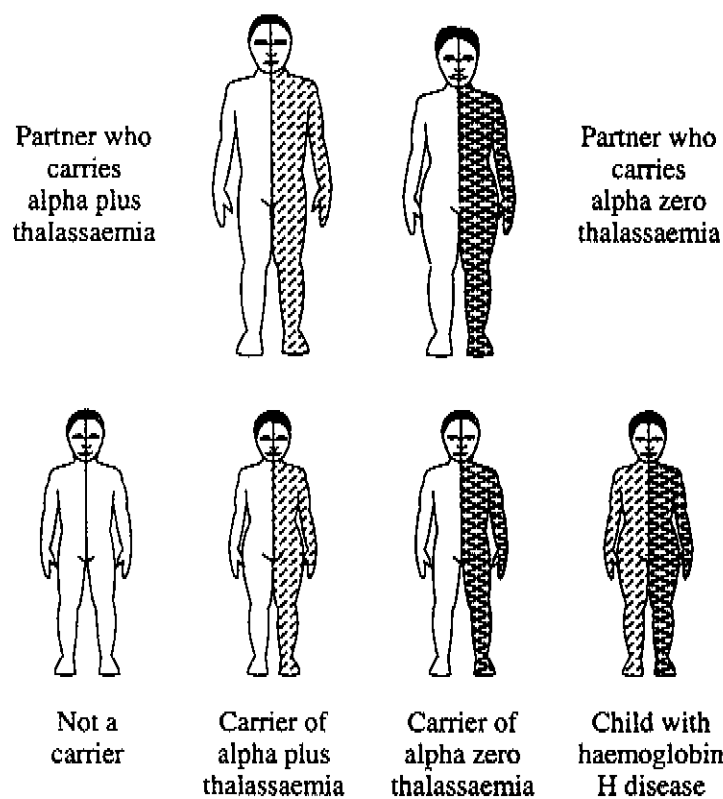
People who inherit alpha thalassaemia from *both* parents may have an anaemia. There are two types of anaemia due to alpha thalassaemia. One form is mild, and one form is severe.

The mild form is *Haemoglobin H disease*. This occurs when a person inherits alpha zero thalassaemia from one parent, and alpha plus thalassaemia from the other parent. This is probably what happened in your case.

The severe form is *Alpha thalassaemia major*. This is also called *haemoglobin Bart's hydrops fetalis*, or *alpha thalassaemia hydrops fetalis*. It is a serious disease of the unborn baby. It occurs only when a baby inherits alpha zero thalassaemia from *both* parents. You do not find adults with alpha thalassaemia major, because it always leads to the death of the baby before, or just after birth. It is described more fully on page 12.

● Since I have haemoglobin H disease, must both my parents carry alpha thalassaemia?

Yes. Most people with haemoglobin H disease have one parent who carries alpha zero thalassaemia trait and one who carries alpha plus thalassaemia trait. When two such people have children, there are four possibilities, shown in the picture opposite.



WHO 94734

- (a) The child may not carry any form of alpha thalassaemia.
- (b) The child may inherit alpha plus thalassaemia from one parent, and no alpha thalassaemia from the other. This child carries alpha plus thalassaemia trait.
- (c) The child may inherit alpha zero thalassaemia from one parent and no alpha thalassaemia from the other. This child carries alpha zero thalassaemia trait.
- (d) The child may inherit alpha zero thalassaemia from one parent and alpha plus thalassaemia from the other. This child has haemoglobin H disease.

In short, in each pregnancy these parents have a 3 out of 4 chance of a child with no anaemia, and a 1 out of 4 chance of a child with haemoglobin H disease.

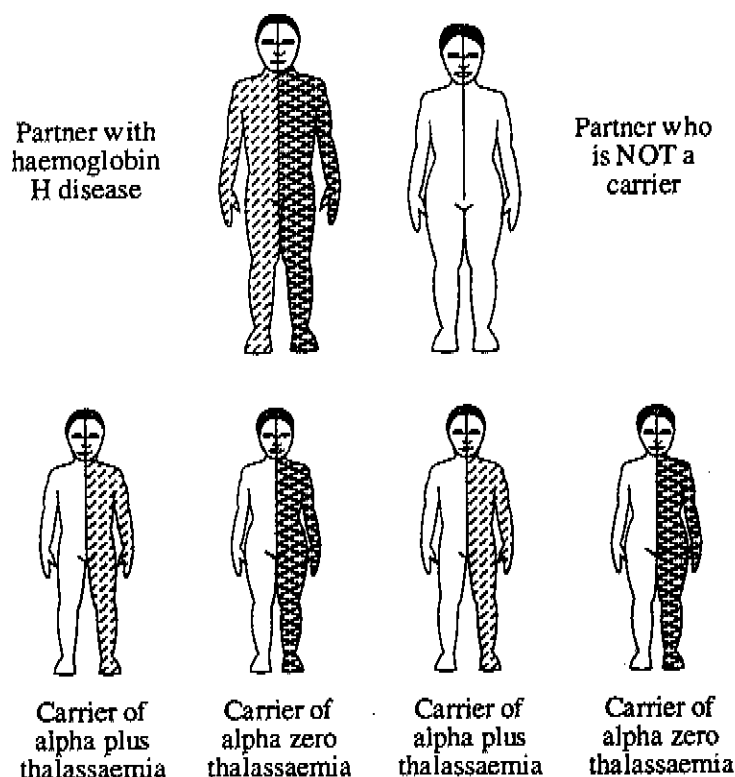
This explains why brothers and sisters in the same family can have different forms of alpha thalassaemia, or even none at all.

3. WILL I PASS HAEMOGLOBIN H DISEASE ON TO MY CHILDREN?

Usually not, but this depends on whether or not your partner carries any form of alpha thalassaemia. It is essential for your partner to have a special blood test to find out. Ideally, this test should be done before you start a pregnancy.

Most people with haemoglobin H disease find that their partner does not carry any form of alpha thalassaemia. In this case none of the children could have an anaemia due to alpha thalassaemia. However, if your partner carries any form of alpha thalassaemia, some of the children could be anaemic. We describe all the possibilities, even though some of them are very rare.

- (a) If your partner does not carry any type of alpha thalassaemia (the most likely situation).



WHO 84735

When one of a couple has haemoglobin H disease and the other does not carry any kind of haemoglobin disorder, in each pregnancy there is a:

1 in 2 chance that the child will carry *alpha zero thalassaemia trait*. This causes no health problem.

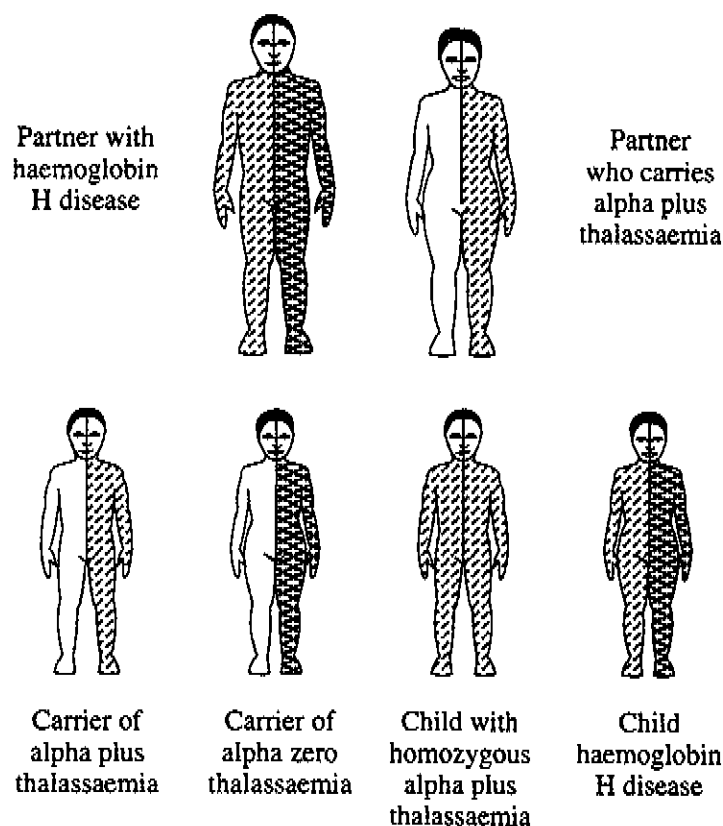
1 in 2 chance that the child will carry *alpha plus thalassaemia trait*. This causes no health problem.

All the children will be just as healthy as those of other couples.

When the children grow up, they should have blood test to see if they carry alpha zero thalassaemia. If they do, and if they choose a partner who also carries alpha thalassaemia, some of their children could suffer from a serious inherited anaemia.

(b) If your partner carries alpha plus thalassaemia.

It is possible that you could have a child with haemoglobin H disease, like yourself.



WHO 94736

In each pregnancy, there is a:

1 in 4 chance that the child will inherit alpha plus thalassaemia from you, and no alpha thalassaemia from your partner. This child will carry alpha plus thalassaemia trait. This causes no health problem.

1 in 4 chance that the child will inherit alpha zero thalassaemia from you, and no alpha thalassaemia from your partner. This child will carry alpha zero thalassaemia trait. This causes no health problem.

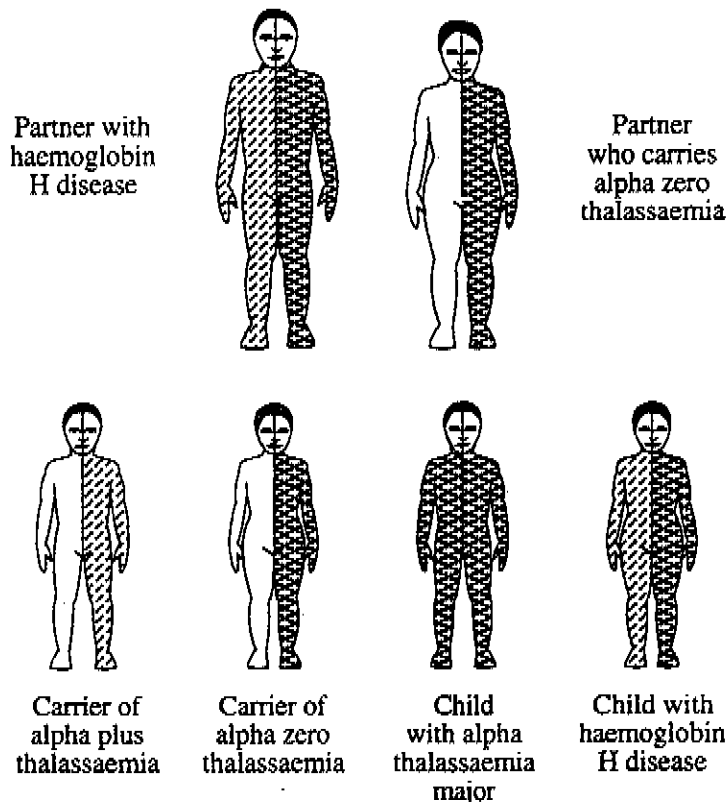
1 in 4 chance that the child will inherit alpha plus thalassaemia from both you and your partner. This child will carry "homozygous alpha plus thalassaemia". This causes no health problem.

1 in 4 chance that the child will inherit alpha zero thalassaemia from you, and alpha plus thalassaemia from your partner. This child will have *haemoglobin H disease*.

When the children are born, they should have a blood test to see if they have haemoglobin H disease or carry alpha zero thalassaemia.

(c) If your partner carries alpha zero thalassaemia.

This is very unlikely, but it could happen. In this case there is quite an important risk. Such a couple could have a baby with *alpha thalassaemia major*. They could also have a child with haemoglobin H disease, like yourself.



In each pregnancy, there is a:

WHO 94737

1 in 4 chance that the child will inherit alpha plus thalassaemia from you, and no alpha thalassaemia from your partner. This child will carry alpha plus thalassaemia trait. This causes no health problem.

1 in 4 chance that the child will inherit alpha zero thalassaemia from you, and no alpha thalassaemia from your partner. This child will carry alpha zero thalassaemia trait. This causes no health problem.

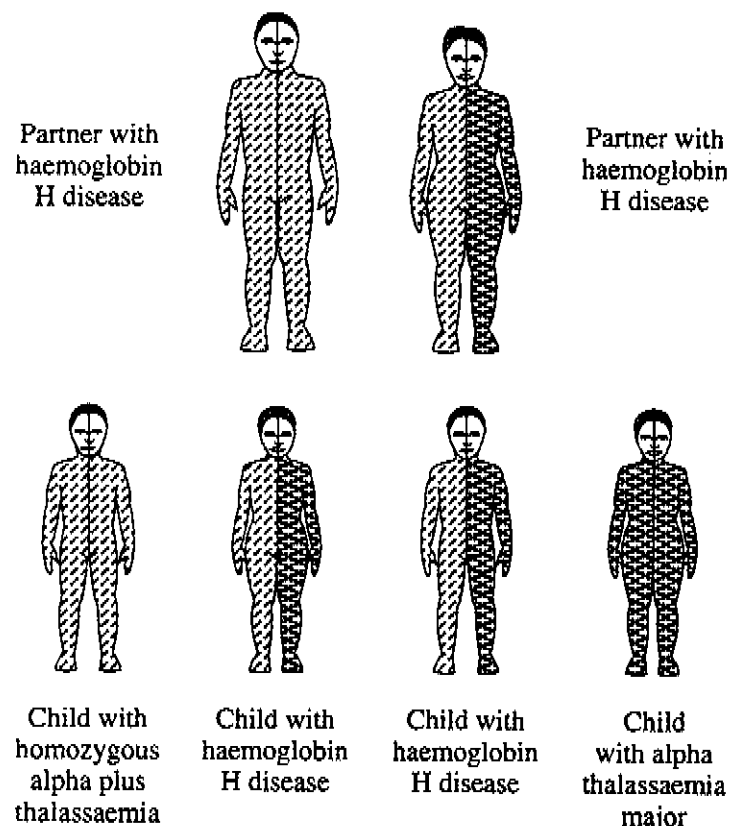
1 in 4 chance that the child will inherit alpha plus thalassaemia from you and alpha zero thalassaemia from your partner. This child will have haemoglobin H disease, like yourself.

1 in 4 chance that the baby will inherit alpha zero thalassaemia from both you and your partner. Such a baby will have *alpha thalassaemia major*.

Alpha thalassaemia major is also called "*Haemoglobin Bart's hydrops fetalis*", and "*alpha thalassaemia hydrops fetalis*". It is a very serious anaemia that always kills the baby before or just after birth. It can also cause risks for the mother. When a baby in the womb has *alpha thalassaemia major*, the pregnancy seems to go quite normally up to about 5 months, sometimes for longer. But then the baby does not grow normally any longer, and the mother may develop high blood pressure. An ultrasound examination (a "scan") usually shows that the baby is "oedematous", which means it is puffed up with water. The mother often develops high blood pressure, and may deliver prematurely. There may be difficulties at delivery, and the baby is dead or dying when it is born.

(d) What could happen if my partner also had haemoglobin H disease?

This is extraordinarily unlikely. If it did happen, the risk is much the same as if your partner simply carried alpha zero thalassaemia trait.



WHO 94738

In each pregnancy, there would be a:

1 in 4 chance that the child would inherit alpha plus thalassaemia from both you and your partner. This child would have " homozygous alpha plus thalassaemia". This causes no health problem.

1 in 2 chance that the child would inherit alpha plus thalassaemia from one parent and alpha zero thalassaemia from the other. This child would have haemoglobin H disease, like the parents.

1 in 4 chance that the baby would inherit alpha zero thalassaemia from both you and your partner. Such a baby would have *alpha thalassaemia major*.

In short, there would be a 1 in 4 risk of a serious problem in the pregnancy.

● **Is it possible that I could have a baby with alpha thalassaemia major?**

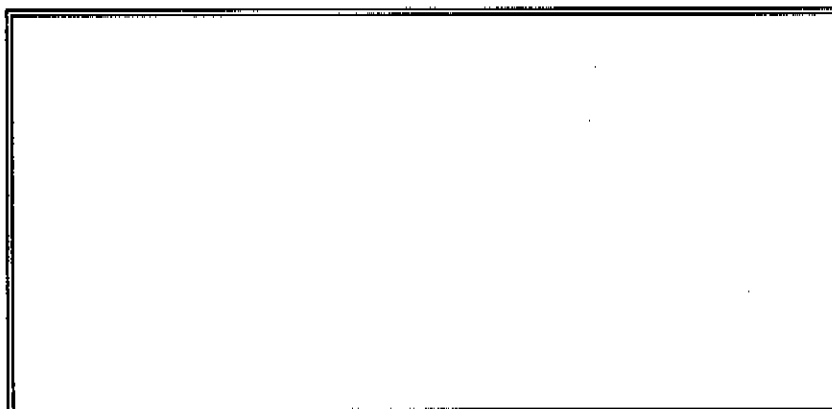
Yes, you could risk having a child with alpha thalassaemia major, *but only if your partner carries alpha zero thalassaemia, or also has haemoglobin H disease*. In such a case, there is a 3 out of 4 chance in every pregnancy that the baby will be unaffected, and a 1 in 4 chance that it will have alpha zero thalassaemia major.

● **Is there any way to avoid having a child with alpha thalassaemia major?**

Yes. It is possible to avoid having a child with alpha thalassaemia major, through *prenatal diagnosis*. Doctors can test the unborn baby at around 10 weeks of pregnancy. If it happens to have alpha thalassaemia major, the pregnancy can be terminated, and the parents can try again to have an unaffected baby.

Most couples who know they could have a child with alpha thalassaemia major wish to avoid the risk. They usually ask for prenatal diagnosis.

If you want to know more about prenatal diagnosis, ask your doctor, or contact your local support association:



4. IS THERE ANYTHING ELSE I SHOULD DO NOW?

- *Make sure that your partner is tested for alpha thalassaemia, ideally before pregnancy.*
- *If you have any brothers or sisters, they could also carry alpha thalassaemia. Encourage them to ask for testing for alpha thalassaemia. If they do carry alpha thalassaemia, the blood should then be tested using DNA methods, to see if they carry alpha zero or alpha plus thalassaemia trait.*
- *Keep this booklet safely with your medical papers.*
- *Make sure you see a specialist in haemoglobin disorders at least once a year. Start using the charts at the end of this booklet to keep a life-long record of your haemoglobin H disease. Enter your haemoglobin level, spleen size (and, for children, height and weight) after every visit to the specialist in haemoglobin disorders.*
- *If you go to see a doctor about your haemoglobin H disease, or you become pregnant and go to see a doctor or a midwife, take this booklet with you.*

PATIENT RECORD FOR HAEMOGLOBIN H DISEASE

This treatment book is meant to be kept by parents (and later by patients themselves). It will help you to control your haemoglobin H disease and will help doctors to understand it. It is also useful when you travel, because doctors can see exactly what your diagnosis and treatment are. As a person with haemoglobin H disease gets older, this treatment record will become more valuable.

Keep this book carefully. Take it with you, and fill it in, every time you visit the haematology clinic.

Contents

	<u>Page</u>
How to use this treatment record	16
Basic information about the patient:	
● Sheet 1	17
● Sheet 2	18
Chart for recording haemoglobin level and spleen size, and any health problem or medical treatment	19
Growth charts (height and weight):	
● Boy	20
● Girl	22

This treatment record is sponsored by:

The Thalassaemia International Federation, Nicosia, Cyprus
The World Health Organization, Geneva, Switzerland

HOW TO USE THIS TREATMENT RECORD

When you first get those notes, fill in all the basic information on sheets 1 and 2, with the help of your doctor.

Your doctor should also write a short summary of your previous history at the bottom of sheet 2.

Starting on page 19, there are a set of charts.

Start filling in the information about each clinic visit. Enter all your haemoglobin measurements with the date. Enter all measurements of height and weight. Enter other information such as treatments you have (folic acid, splenectomy). Enter when you get married, and when you have children.

Make sure that your notes have the right growth-chart for a boy or a girl. Heights and weights can most easily be charted by using a transparent ruler. The lines marked 'longitudinal standards' represent the percentiles for children followed at successive ages. The standards of normality taken must depend on the purpose for which they are being used. They also depend on the level of the average values obtained in a given clinic; regional variations may require a slight shifting of the scale from place to place.

Children should be weighed and measured every 6 months, and adults should be weighed every 6 months either at home or at the hospital. Write the measurements on the chart. You can also enter the measurements directly on the growth chart. If you are not sure how to do this, discuss it with your doctor or nurse.

BASIC INFORMATION - SHEET 1

1. First Name: Diagnosis:
Family Name: Full Blood Group:
Date of Birth: Identification Number:
Address:
Telephone:

2. Are you allergic to penicillin? YES NO
Are you allergic to any other drug? YES NO
If yes, which drug:
Do you have any red cell antibodies? YES NO
If yes, which ones:

3. Family Doctor:
Address:
Telephone:

4. Usual Hospital Clinic:
- Doctor
- Hospital
- Address
- Telephone Number

5. Specific Alpha Thalassaemia Mutations:
- Mother
- Father
- Patient

