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**EDUCATIONAL MATERIALS**

**ON**

**HAEMOGLOBINOPATHIES:**

***ALPHA ZERO THALASSAEMIA***

(Restricted for Clinicians and for Distribution via DNA Laboratories Only)



WORLD HEALTH ORGANIZATION  
HEREDITARY DISEASES PROGRAMME  
1994

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**IMPORTANT NOTE**

This booklet provides information on alpha zero thalassaemia trait. It is important that this booklet is given only to people who have had a definitive diagnosis of alpha zero thalassaemia trait by DNA methods. It should be distributed only by laboratories performing DNA tests. If it is given out in any other context, there is a risk that it will be given to a carrier of alpha plus thalassaemia, who has no reproductive risk. This would amount to serious misinformation and it is better to give no information than to misinform.

The booklet is intended to be sent out by the DNA laboratory whenever a definitive diagnosis of alpha zero thalassaemia trait is made. The molecular biologist should enter details of the diagnosis in the table provided on page 3. If the person has a partner, details of their blood test results should also be entered in the table. The counsellor should hand the booklet to the patient.

*This booklet is provided by WHO as a draft only,  
and it should be specifically adapted to the needs of each country.*

## INFORMATION ON ALPHA ZERO THALASSAEMIA TRAIT

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## 1. INTRODUCTION

There are several kinds of thalassaemia.

This booklet is for people who have had a blood test that definitely shows they carry alpha zero thalassaemia trait.

Important points to remember about alpha zero thalassaemia trait.

- Alpha zero thalassaemia trait is not an illness, and does not affect your health.
- Alpha zero thalassaemia trait is passed on to their children by men as well as women.
- Alpha zero thalassaemia trait is different from beta ( $\beta$ ) thalassaemia trait
- Your alpha zero thalassaemia trait could affect the health of your pregnancies, but you can avoid this risk with medical advice.
- Do not forget that you carry alpha zero thalassaemia trait. Keep your blood test results and this booklet, with your medical papers.
- Show this booklet to your doctor when you are thinking of having a family, or when he or she takes blood for any other reason.
- Show this booklet to your family doctor when you think you may be pregnant.
- Show this booklet to the midwife and doctor when you attend an antenatal clinic.
- If you want more information, ask your doctor to arrange a visit to a special thalassaemia counsellor, or a genetic counsellor.

*Take this booklet with you if you go to see a doctor or counsellor about your alpha zero thalassaemia trait.*

**2. BLOOD TEST RESULTS**

The molecular biologist who makes the diagnosis should enter the blood test results for the individual (and their partner), provide the relevant administrative details requested and sign where indicated in the table shown below.

**To whom it may concern:**

The carrier of this booklet has been found to carry alpha zero thalassaemia trait. Blood test results are given in the table below.

Their partner should have a blood test for thalassaemia, preferably before a pregnancy is started, and the result should also be entered in the table. If this blood test shows any unusual red cell finding, the couple should be referred for expert assessment and genetic counselling.

Further information and testing can be arranged through the centres mentioned in Annex 1:

**BLOOD TEST RESULTS**

NAME	DATE OF TEST	Hb	MCH	MCV	Hb Electrophoresis	% Hb A <sub>2</sub>	DNA STUDIES
(OF PATIENT)							
(OF PARTNER)							

**NAME AND ADDRESS OF CENTRE ARRANGING THE TEST:**

Telephone No.:

Facsimile No.:

Signature of Doctor/Counsellor

FULL NAME IN CAPITAL LETTERS

Place and Date:

### 3. WHAT IS ALPHA ZERO THALASSAEMIA ?

Alpha zero thalassaemia trait is a characteristic of the blood. It is inherited, that is, it is passed on from parents to children 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.

Alpha zero thalassaemia is common among people originating from South East Asia. It occurs occasionally among people originating from the Mediterranean area or the Middle East, and very rarely in North Europeans. For example, about 1 in 15 people originating from Southern China, 1 in 50 Cypriots, and 1 in 1,000 North Europeans carry alpha zero thalassaemia trait.

There are three forms of alpha zero thalassaemia.

- **Alpha zero thalassaemia trait.** People with alpha zero thalassaemia trait are perfectly healthy in themselves, but if both members of a couple carry alpha zero thalassaemia trait, they may pass alpha zero thalassaemia major on to their children.
- **Alpha zero thalassaemia major.** This can happen if a baby inherits alpha zero thalassaemia from both parents. It is a very severe anaemia that affects the unborn baby in the womb. The baby cannot make enough blood, and dies either before birth, or a few minutes afterwards. Alpha zero thalassaemia major is also called **alpha thalassaemia hydrops fetalis** or **haemoglobin Bart's hydrops fetalis**.
- **Haemoglobin H disease.** This can happen when one parent has alpha zero thalassaemia trait and the other has a milder form of alpha thalassaemia called alpha plus thalassaemia trait. People with haemoglobin H disease are anaemic, but can usually lead a normal life without the need for any treatment. See p 7 for more details.

### 4. BLOOD AND ANAEMIA

To explain about alpha thalassaemia we must talk a little about normal blood and anaemia.

Blood is made up of a lot of blood cells in a clear slightly yellow liquid called plasma. Blood is red because the red blood cells contain a substance called haemoglobin, which carries oxygen from your lungs to wherever it is needed in your body. Haemoglobin contains a lot of iron. The main reason why people need iron in their food is to make haemoglobin.

#### What is anaemia ?

Some people have too little haemoglobin in their blood. These people have anaemia. There are many different kinds of anaemia. The most common kind is iron deficiency anaemia. This happens when people are not eating enough of the foods that contain iron, or if people lose a lot of blood by bleeding. Some people who carry thalassaemia have a very mild anaemia, but it has nothing to do with the amount of iron you are getting from your food.

Thalassaemia is not iron deficiency anaemia. It is an inherited condition. However, people with alpha zero thalassaemia trait can also get iron deficiency. People with alpha zero thalassaemia trait and people with iron deficiency anaemia have smaller red blood cells than usual.

### How do you find out if you have alpha zero thalassaemia trait?

You have to have a special blood test, called a DNA test, which has to be done at a special laboratory. Your results should be written inside the cover of this booklet.

## 5. WHAT DOES ALPHA ZERO THALASSAEMIA TRAIT MEAN FOR ME ?

### ● Is an alpha zero thalassaemia carrier ill ?

No. Thalassaemia carriers are not more likely to get other illnesses. Thalassaemia trait does not make them weak, and they can do any kind of job they want.

### ● Is there any treatment to get rid of alpha zero thalassaemia trait ?

No, if you are born with thalassaemia trait you will always have it.

### ● Can alpha zero thalassaemia trait turn into a more severe form of thalassaemia ?

No, it cannot.

### ● Is alpha zero thalassaemia trait catching ?

No, it is not.

### ● Do alpha zero thalassaemia carriers ever need iron ?

Yes, they sometimes do, because they can also get iron deficiency anaemia like other people. Then they may need iron medicine. But it is important that you only have iron medicine if you really need it. The best way to tell whether a thalassaemia carrier needs iron is by a blood test that measures the amount of iron in your blood. (A serum iron or serum ferritin measurement). If you do not have this test, it may appear that you are short of iron simply because you have small red blood cells, and you may be advised to keep taking extra iron even when you do not need it. This will do you no good, and in the long-run it could be harmful.

### ● What about pregnant women ?

Pregnant women with alpha zero thalassaemia trait may need extra iron in the same way as any other pregnant women.

### ● Why is alpha zero thalassaemia trait found in certain countries ?

People with any kind of thalassaemia trait are less likely to die if they get malaria. In the past, in countries where malaria was common, people with thalassaemia trait survived malaria when other people died, so carrying thalassaemia gave them an important advantage. These people passed thalassaemia on to their children, so as time passed thalassaemia trait became common in malarious parts of the world. Now we can usually cure or prevent malaria, so thalassaemia trait is less of an advantage. Because it is inherited, it does not go away from a population when malaria disappears, or from people born in another part of the world.

● Does alpha zero thalassaemia trait have any other advantage ?

Probably. It seems that people who carry thalassaemia may be less likely than other people to suffer from heart attacks when they get older.

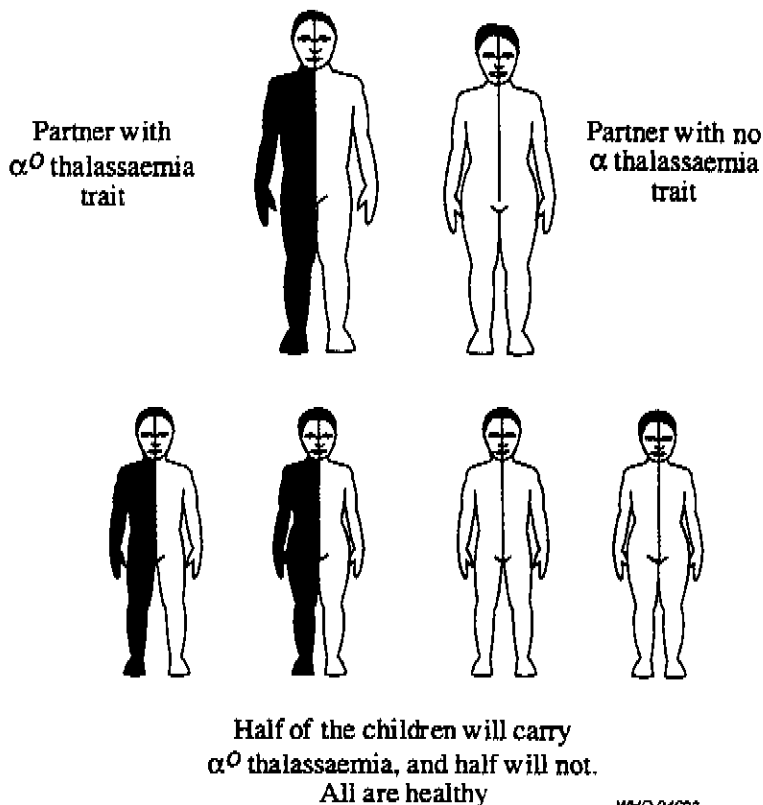
6. **WHAT COULD MY ALPHA ZERO THALASSAEMIA MEAN FOR MY CHILDREN ?**

It is important to know that you carry alpha zero thalassaemia trait, because sometimes carriers can have children affected by alpha zero thalassaemia major. This is a serious disease of the unborn baby. If you become pregnant with a baby with alpha thalassaemia major, you could get raised blood pressure and have difficulties at delivery.

To explain more about this risk, we must see how alpha zero thalassaemia is passed on from parents to their children. Let us consider three sorts of couples.

- A. A carrier of alpha zero thalassaemia trait has a partner who does not carry any kind of alpha thalassaemia. This is the commonest situation. There is no problem for an alpha thalassaemia carrier whose partner is not a carrier.

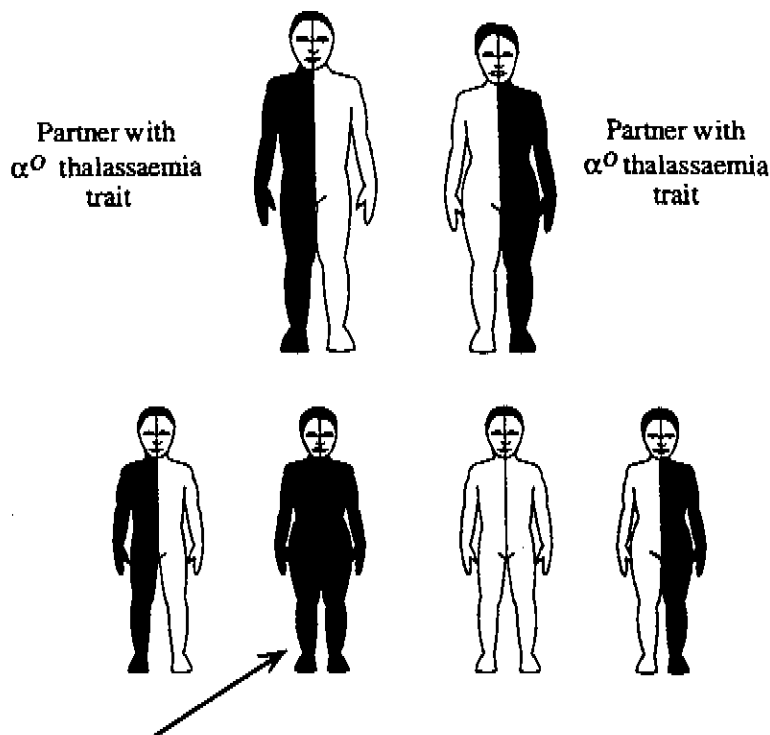
In each pregnancy there is a 1 in 2 chance that the child will carry alpha zero thalassaemia trait, and a 1 in 2 chance that it will not. None of the children can have alpha thalassaemia major. The mother will have no particular additional problems during pregnancy due to alpha zero thalassaemia trait.



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- B. Occasionally, a carrier of alpha zero thalassaemia trait chooses a partner who also carries alpha zero thalassaemia trait.

In each pregnancy there is a 1 in 4 chance of a baby with alpha zero thalassaemia major, and a three out of four chance that the baby will be healthy.



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### ● What is Alpha Zero Thalassaemia Major ?

Other names for alpha zero thalassaemia major are alpha thalassaemia hydrops fetalis, and Haemoglobin Bart's hydrops fetalis.

This is a very serious anaemia that develops in the unborn baby. It can only happen when both parents carry alpha zero thalassaemia trait.

The unborn baby cannot make enough haemoglobin, and becomes very anaemic. It becomes weak and its heart cannot pump blood around properly. The pregnancy seems to go normally up to about five months, sometimes for longer, but then the baby stops growing normally, and the mother may develop high blood pressure. An ultrasound examination (a scan) may be done. This usually shows that the baby is "oedematous" - which means that it is puffed up with water. Usually the mother starts labour early, between 28 and 36 weeks of pregnancy, and the baby is dead or dying when it is delivered.

There is a one in four chance of the same thing happening in any further pregnancies. This problem can be avoided. This is why it is so important for people who have alpha zero thalassaemia trait to find out whether their partner also carries it, before they have a family.

● Can alpha zero thalassaemia major be treated ?

There is no treatment for alpha zero thalassaemia major.

● Can alpha zero thalassaemia major be prevented ?

Yes. When both parents carry alpha zero thalassaemia trait, there are several ways to avoid having a stillborn baby.

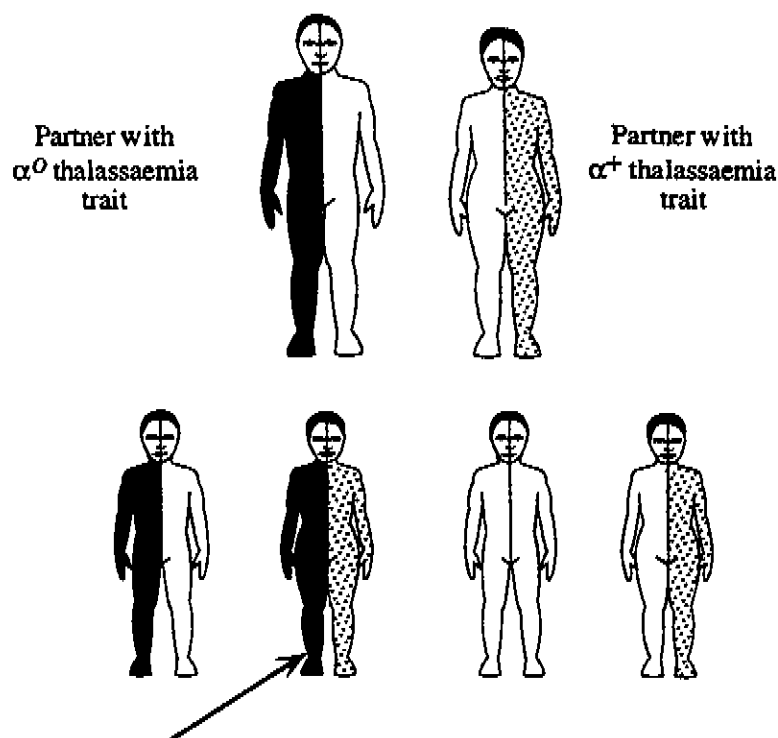
It is possible to test the unborn baby very early in a pregnancy, to see whether it is healthy, or suffers from alpha zero thalassaemia major. This test is called prenatal diagnosis. It can be done at any time after 9 weeks of pregnancy.

When prenatal diagnosis shows the fetus is affected, the parents usually choose to have the pregnancy terminated because the baby has no hope of a normal life. Then they start another pregnancy, hoping to have a healthy child this time. Remember, there is a three out of four chance of a healthy child in each pregnancy!

There are several other ways to avoid having children with alpha zero thalassaemia major. To find out more, ask your doctor to arrange for you to visit a genetic counsellor or a haemoglobinopathy counsellor.

C. Sometimes a person with alpha zero thalassaemia trait chooses a partner with alpha plus thalassaemia trait.

Alpha plus thalassaemia trait is also called the harmless form of alpha thalassaemia trait, because it can only cause problems when it is combined with alpha zero thalassaemia trait. When one of a couple carries alpha zero thalassaemia trait and the other carries alpha plus thalassaemia trait, most of their children will be completely healthy. But there is a one in four chance for each child to inherit alpha zero thalassaemia from one parent and alpha plus thalassaemia from the other. This leads to haemoglobin H disease (Hb H disease).



One out of 4 children (on average) may inherit  $\alpha^0$  thalassaemia from one parent and  $\alpha^+$  thalassaemia from the other.

This child will have **haemoglobin H disease**.

All the other children will be healthy.

● What is haemoglobin H disease ?

People with haemoglobin H disease are anaemic: their haemoglobin level is considerably lower than normal. All the same, most people with haemoglobin H disease are quite well, can work and have children like other people, and do not need any special treatment.

Most couples who could have children with haemoglobin H disease are not really worried. They usually ask to have the baby tested as soon as it is born, so that they can know the situation. If the baby does have Hb H disease, the parents are advised to attend a regular clinic a few times a year, just to check that the baby is growing well, and make sure that there are no problems.

7. **OTHER HAEMOGLOBIN DISORDERS**

Beta thalassaemia trait

This is also common in most of the populations where alpha thalassaemia trait occurs.

When people talk about thalassaemia they usually mean beta thalassaemia, because it was known about before alpha thalassaemia, and because it causes problems more often than alpha thalassaemia. It is described in a separate booklet "Everything you need to know about beta thalassaemia trait", which can be obtained from The UK Thalassaemia Society, 107 Nightingale Lane, GB-London N8, UK (telephone + 44 81 348 0437).

Abnormal haemoglobin

There are a very large number of abnormal haemoglobin (more than 500), but there are only four common types. These are:

- HbS
- HbC
- HbD
- HbE

● What should I do if my partner carries beta thalassaemia trait or an abnormal haemoglobin ?

Sometimes a person with alpha zero thalassaemia trait has a partner who carries beta thalassaemia trait or an abnormal haemoglobin such as Hb S,C, D or E. It is possible for someone who carries one of these to carry alpha thalassaemia trait as well. So if your partner carries one of these, he or she should also have a DNA test for alpha thalassaemia. If he or she does not carry alpha thalassaemia, there is practically no risk that your children could have a severe anaemia due to alpha thalassaemia.

In conclusion, remember that important problems can only ever arise for an alpha zero thalassaemia carrier if they choose another alpha zero thalassaemia carrier as a partner. Even then, problems are uncommon.

8. **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. For instance, your brothers and sisters each have a 1 in 2 chance of being a carrier. Show them this booklet, and advise them to ask for a blood test for alpha zero thalassaemia trait before they have children.

\* \* \* \* \*

ANNEX 1

*List of National Expert Diagnostic Centres*