

EDUCATIONAL MATERIALS
ON
THALASSAEMIA

Thalassaemia is not only a disease of 'just a few people'. It may be your disease, only you don't know it.

Thalassaemia is a serious illness that is handed on to their children by parents who do not know that they are 'healthy carriers'.

Thalassaemia can be prevented if information, scientific research and proper medical services can be made available.

COUNSELLING BOOKLET FOR SINGLE HETEROZYGOTES

What you need to know about

THALASSAEMIA TRAIT

Dear Reader,

You have been given this booklet because you have been told that you carry thalassaemia trait. The booklet will give you a lot of information about thalassaemia trait, but these are the points that matter most.

- * Your thalassaemia trait is not an illness and does not affect your own health. However, it could affect the health of your future children.
- * Do not forget that you carry thalassaemia trait. Keep your blood test results among your personal documents.
- * There is nothing bad about carrying thalassaemia trait. There is no need to feel embarrassed or ashamed about it. Instead, talk about it with your partner and family and if they haven't already had a blood test, persuade them to go for one.
- * If your partner (present or future) does not carry thalassaemia trait, there is no danger. However, your children may be carriers like yourself. They should have their blood tested at some time before they have children of their own.
- * If both you and your partner are carriers of thalassaemia trait, there is a danger for your future children, but you can avoid it by family planning.
- * If you want more information after you have read this booklet, ask your doctor to arrange a visit to a genetic counsellor.

Take this booklet with you if you go to see your doctor about your thalassaemia trait.

This is a booklet for people who have had a blood test that shows they carry beta thalassaemia trait. For short, this is called thalassaemia trait. If you have picked up the booklet by chance, please read it anyway. You might find that you should have a blood test to see if you carry thalassaemia trait yourself.

What is thalassaemia?

Thalassaemia is a peculiarity of the blood that is found in many countries around the world, and particularly in people of Mediterranean, Middle Eastern and Asian origin. It is rare in Northern Europeans.

There are two forms of thalassaemia:

1. Thalassaemia trait. People with thalassaemia trait are perfectly healthy themselves but they can pass thalassaemia major on to their children.

*There are about 200,000 people with thalassaemia trait in Britain. They are sometimes called "healthy carriers of thalassaemia".

Thalassaemia trait is sometimes called thalassaemia minor.

2. Thalassaemia major. This is a very serious blood disease which begins in early childhood. Children who have thalassaemia major cannot make enough haemoglobin in their blood. They need frequent blood transfusions and medical treatment.

Every year at least 100,000 children are born in the world with thalassaemia major. *In Britain, there are about 300 young people with the disease.

Thalassaemia major is sometimes called Mediterranean Anaemia, Cooley's Anaemia, or Homozygous Beta Thalassaemia.

Blood and anaemia

To understand more about thalassaemia, you need to know a little about normal blood and about anaemia.

What is blood made of?

Blood is made up of a lot of red blood cells in a clear, slightly yellow liquid called plasma. Each red blood cell only lives for about 4 months. It is then broken down. New blood cells are being made all the time. The blood cells are replaced very quickly - that's why people can give blood often.

Blood is red because the red blood cells contain a substance called haemoglobin. Haemoglobin is very important because it carries oxygen from your lungs to wherever it is needed in your body.

Haemoglobin contains a lot of iron. When your red blood cells are broken down, most of the iron from the haemoglobin is used again to make new haemoglobin. You lose some iron from your body in your urine and you make up for it with the iron in the food you eat. In fact, 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 do not have enough haemoglobin because they're not eating enough of the foods that contain iron.

Thalassaemia major is a different kind of anaemia. It is caused by not having enough haemoglobin, but it has nothing to do with the amount of iron you're getting from your food. It is an inherited disease.

*Insert here the appropriate figures for the country.

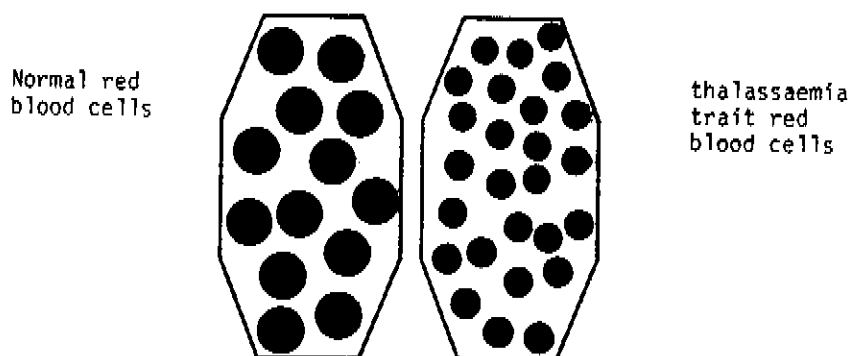
THALASSAEMIA TRAIT

What is thalassaemia trait?

People with thalassaemia trait carry thalassaemia but they are not ill. They are absolutely healthy and normal but some of them have slight anaemia.

Most people with thalassaemia trait do not know that they have it. You only discover if you have a special blood test, or if you have a child with thalassaemia major.

The red blood cells of people with thalassaemia trait are smaller than usual.



People with thalassaemia trait also have slightly more of a kind of haemoglobin called haemoglobin A₂ in their blood. Thalassaemia trait is present at birth, it remains the same for life, and it can be handed on from parents to children. That means, it is inherited.

Why does it matter if you carry thalassaemia trait?

It is important to know if you carry thalassaemia trait because sometimes people with thalassaemia trait can have children with thalassaemia major, a serious blood disease.

How do you find out if you have thalassaemia trait?

You have to have a special blood test. The doctors can tell by measuring the size of your red blood cells and how much haemoglobin A₂ you have in your blood.

Is a thalassaemia carrier ill?

No. So there is no need for any special medical treatment.

Is a thalassaemia carrier more likely to get other illnesses?

No.

Is a thalassaemia carrier physically or mentally weak?

No.

Does thalassaemia trait affect the sort of work you can do?

No.

Can any treatment change thalassaemia trait?

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

Can thalassaemia trait turn into thalassaemia major?

No.

Do thalassaemia carriers ever need iron medicine?

Yes, they sometimes do, but it's 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 special blood test that measures the amount of iron in your blood. If you don't have this test, the doctor may think that you are short of iron simply because you have small red cells and slight anaemia, and may advise you to keep taking extra iron when you really 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 thalassaemia need extra iron just as much as any other pregnant woman.

Why is thalassaemia trait found in certain countries?

People with thalassaemia trait are less likely to die if they catch malaria. In the past, in countries where malaria was very common, people with thalassaemia trait survived malaria when other people died. They passed the trait on to their children. So thalassaemia trait was a great advantage and as time passed it became more common in malarial parts of the world. But now we can cure or prevent malaria, and thalassaemia trait is no longer an advantage. It does not go away when malaria disappears.

Very many countries used to have malaria and all now have quite a large number of people with thalassaemia trait. For instance, in Cyprus one in seven people has thalassaemia trait (both Turkish and Greek Cypriots), and in Greece one in twelve people has thalassaemia trait. In Italy and all of the Middle East and Asia, including India, Pakistan, Hong Kong and Vietnam, the number of people with thalassaemia trait varies from one in fifty to one in ten in different areas. In Africa and the West Indies about one in fifty people has thalassaemia trait. About one in every thousand people of British origin has the trait.

Other forms of thalassaemia trait

This booklet is all about beta-thalassaemia trait, but there are other forms of thalassaemia trait:

Delta-beta thalassaemia trait and Haemoglobin Lepore trait are very similar to beta-thalassaemia trait. If you have either of these traits, all the information in this booklet applies to you.

Alpha-thalassaemia trait is very different from beta-thalassaemia trait. It is not common and only rarely causes any illness in children. People with alpha-thalassaemia trait do not carry beta-thalassaemia trait. This booklet does not apply to them.

In addition to the thalassaemias there are three important forms of abnormal haemoglobins. These are:

Haemoglobin S

Haemoglobin C

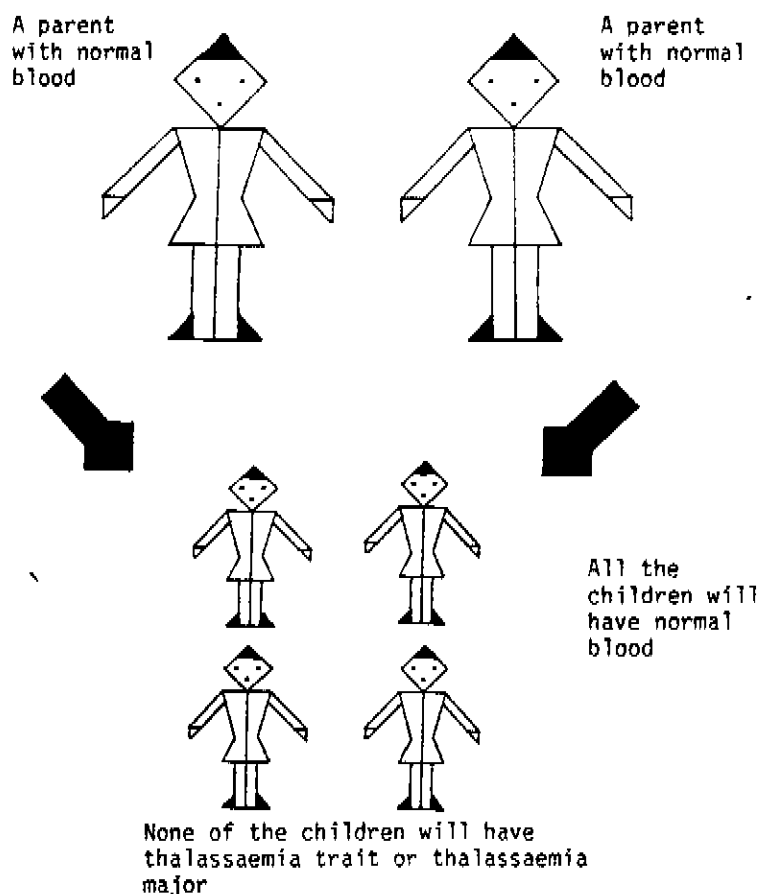
Haemoglobin E.

If someone who carries beta-thalassaemia marries someone who carries one of these abnormal haemoglobins, there is a risk that some of the children could have a serious anaemia, like thalassaemia major.

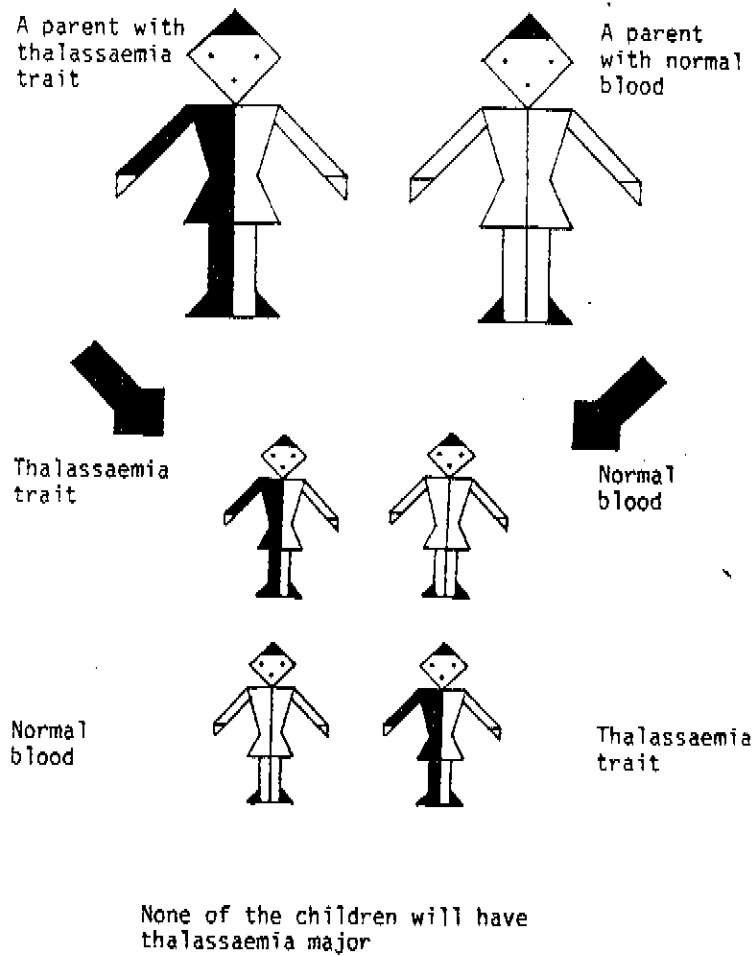
How is thalassaemia trait passed on from parents to their children?

Let us consider three sorts of couples.

1. If both parents have normal blood, they cannot possibly pass on thalassaemia trait or thalassaemia major to their children. All their children will have normal blood.



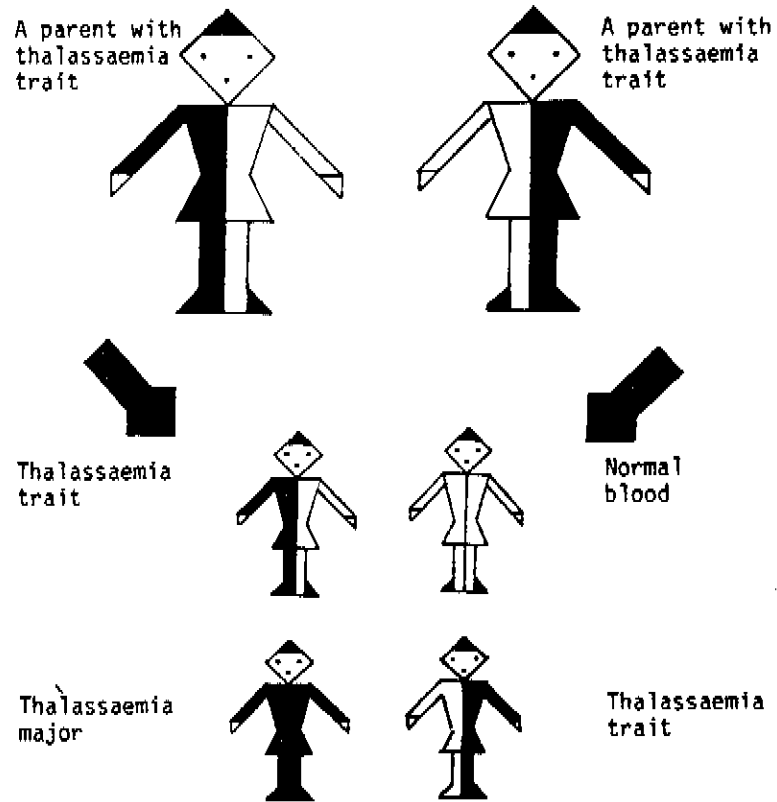
2. If one parent has a thalassaemia trait and one has normal blood there is a one in two (50%) chance that each of their children will have thalassaemia trait. None of their children can have thalassaemia major.



People with thalassaemia trait are completely healthy, so they can pass on the trait through many generations without anybody realising that it is "in the family".

3. If both parents carry thalassaemia trait, their children may have thalassaemia trait, or they may have completely normal blood, or they may have thalassaemia major.

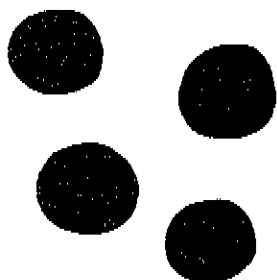
In each pregnancy there is a one in four (25%) chance that their child will have normal blood, a two in four (50%) chance that the child will have thalassaemia trait, and a one in four (25%) chance that the child will have thalassaemia major.



THALASSAEMIA MAJOR

What is thalassaemia major?

Thalassaemia major is a serious inherited childhood anaemia. Children with thalassaemia major cannot make enough haemoglobin. Because of this their bone marrow cannot produce enough red blood cells. The red blood cells that are produced are nearly empty.



Normal Red Blood Cells



Thalassaemia major
red blood cells

Children with thalassaemia major are normal at birth but become anaemic between the ages of three months and eighteen months. They become pale, do not sleep well, do not want to eat, and may vomit their feeds. If children with thalassaemia major are not treated, they have miserable lives. They usually die between one and eight years old.

Can thalassaemia major be treated?

The only treatment for thalassaemia major is regular blood transfusions, usually every four weeks. Most children who have these transfusions grow normally and live quite happily into their early twenties. But to live longer, they need other treatment as well.

After each blood transfusion the red blood cells in the new blood are broken down slowly over the next four months. The iron from the red blood cells stays in the body. If it is not removed, it builds up and can damage the liver, the heart and other parts of the body. If this damage is not prevented most people with thalassaemia major die when they are about twenty years old.

At present the only way to remove the extra iron from the body is to give injections of a drug called Desferal under the skin from a small pump 5-7 nights of every week. Desferal picks up the iron and carries it out in the urine. This treatment is very successful and most children treated with blood transfusions and Desferal can now lead fairly normal healthy lives. We hope that they will be able to work, marry and have children. But the treatment is unpleasant and often upsetting. We are looking for better treatment all the time.

How can we prevent thalassaemia major?

If you have thalassaemia trait, that is, if you are a healthy carrier of thalassaemia, when you have children there are two possibilities:

- * If your partner has normal blood, there is no chance that your children could have thalassaemia major, though they could have thalassaemia trait.
- * If both you and your partner have thalassaemia trait, then in each pregnancy there is a one in four chance that you will have a child with thalassaemia major.

When both partners carry thalassaemia trait, there are several ways to avoid having sick children. For instance, the doctors can now test for thalassaemia major very early on in the pregnancy while the baby is still in the womb. Many couples who both carry thalassaemia trait decide to test each pregnancy to find out if the baby has thalassaemia major. If it has, they often decide to stop the pregnancy. There are several other ways to avoid having children with thalassaemia major. To find out more ask your doctor to arrange for you to visit a genetic counsellor.

The United Kingdom Thalassaemia Society was formed by the parents of thalassaemic patients in Britain. The aim of the society is to help affected families keep in touch with each other, to raise funds to support research, to improve treatment facilities and to encourage blood testing and counselling and screening programmes.

We are grateful to Alix Henly, and Dr Margaret Jones and Rosie Leyden of the UK Health Education Council for their help with the design of this booklet.

COUNSELLING BOOKLET FOR MARRIED COUPLES OF HETEROZYGOTES

THALASSAEMIA AND FETAL DIAGNOSIS

Dear Parents,

By the time you read this booklet you will already know that you are both healthy carriers of thalassaemia and have a one-in-four chance of having a child affected by this disease. (If you have picked up this booklet by chance - Have you been tested for thalassaemia? Do you know whether you are a carrier? If not you should know that in our country * in * people are healthy carriers of this disease - so there is a chance that you are a carrier. There are no symptoms or characteristics which can warn you of this).

Carrier couples

When two carriers have a child, there is a 1 in 4 chance that the child will have thalassaemia major. This chance is the same in each pregnancy. You cannot know in which pregnancy or in which order the affected children will come.

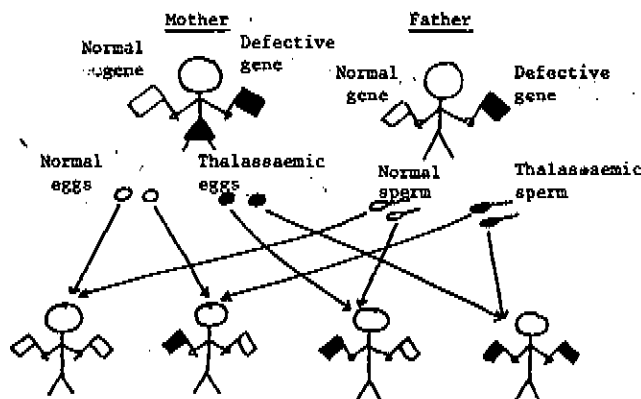
You see, being a carrier means that one of the two "genes" that control the production of the haemoglobin in your red blood cells is defective. Since the other gene is functioning well you are healthy.

When a child is being formed it will inherit one gene from each parent. From a parent who is a carrier it can receive either the defective gene or the functioning one.

If the baby receives both functioning genes - one from each parent - it will be normal.

If it receives one functioning gene and one defective one it will be a carrier like you.

If both parents are carriers then there is the possibility - remember a 1 in 4 chance - that it will inherit both defective genes. In this case the child will be anaemic - it will not be able to produce enough haemoglobin for its blood cells. It will have thalassaemia major.



This child has inherited 2 functioning genes and is normal

These two children have inherited one functioning and one defective gene. They are carriers like their parents

This child has inherited 2 defective genes and is anaemic

(1/4 chance, or 25%) (2/4 chance, or 50%)

(1/4 chance, or 25%)

When the mother produces eggs (once a month) the egg is either completely normal or completely thalassaemic. There is no way of telling in which order they will come.

And when the father produces sperm, half are completely normal and half are thalassaemic.

*Insert here the appropriate figures for the area.

If the mother produces a normal egg, it does not matter what kind of sperm meets it. If the normal egg meets a normal sperm the child will be completely normal. If the normal egg meets a thalassaemic sperm the child will be only half thalassaemic - a healthy thalassaemia carrier like yourself.

But what happens if the mother produces a thalassaemic egg? If the thalassaemic egg meets a normal sperm the child will be a healthy carrier of thalassaemia - just like yourself. But if the thalassaemic egg meets a thalassaemic sperm, the child will have thalassaemia major.

The affected child

What is the life of a thalassaemic child like?

What is thalassaemia major?

We have already mentioned that children who suffer from this disease cannot make enough haemoglobin in their blood. They are normal at birth and for the first few months, but usually from around the age of six months, they become very pale, lose their appetite, lose weight and become restless and miserable. If they are not treated they remain pale and weak and develop deformities of their bones with characteristic facial features. Also they have thin limbs and a big belly, because their liver and spleen swell up. They die very young.

Nowadays we can treat these children so that they can live better and longer lives. This treatment consists mainly of regular transfusions of blood - about once a month - for all their life. Also a drug called Desferal has to be injected slowly under the skin for 8-10 hours almost every night. There are also tablets to be taken and regular blood tests. None of these is a cure, which we hope will be found one day, but treatment which will keep the children well for as long as possible. We hope that now they will live healthy lives and be able to work, marry and have their own children. However, the treatment is unpleasant and painful both for the children and their parents.

Prevention

If you and your partner are both carriers:

How can you avoid this problem?

If you do not wish to face the problems and pains of having a thalassaemic child then you have three choices.

First, you may choose to separate. This is a choice open to those not already married and not yet fully committed to a partner. You will then have to find a partner who is not a carrier. A carrier and a non-carrier cannot produce a child with thalassaemia major.

Second, you may choose to stay together but not have children. You could adopt a child. You may even choose to have artificial insemination - the fertilisation of the woman's ovum (egg) by sperm taken from a donor other than the partner (the donor must have been tested and found to be a non-carrier).

Third, you may wish to go ahead and have children of your own. In order to avoid having a thalassaemic child the woman can ask for fetal diagnosis in each pregnancy.

What is fetal diagnosis?

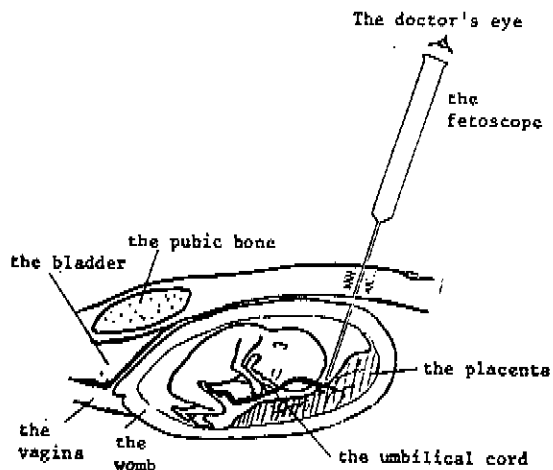
This is a test that can be done in the baby before it is born to see whether it is affected by the disease or not. If it is, then the pregnancy can be terminated. If not then the pregnancy can continue normally. Remember, there is a 3 out of 4 chance of a healthy child in each pregnancy, so most pregnancies continue normally after the test. You will need to go through the test in every pregnancy.

There are couples who have built up a family of 3 or 4 healthy children using this test each time.

There are three different ways to do the test. They are called "fetoscopy", "amniocentesis" and "chorionic villus sampling". Which test you have depends on the methods they use in the laboratory where they study the material from the pregnancy, and on the time in pregnancy when you go to see the doctor. The doctor will explain why a particular test is best for you.

WHAT IS FETOSCOPY?

This is done at 18-20 weeks after the last menstrual period. The doctor, using a very thin needle, takes a few drops of blood from the baby's umbilical cord. The needle does not touch the baby itself. For this to be done, the womb and the baby have to be big enough for an instrument called a fetoscope to be put safely into the womb cavity, and so that it does not harm the baby to take a little blood. The fetoscope is like a rather long needle with a sort of telescope at the end for the doctor to look through, to see inside your womb.



The woman is usually asked to come to the hospital some days before the test for an ultrasound examination. This gives a television picture of the baby and its cord and the placenta. This is painless and harmless. It allows the doctors to plan the test exactly. The mother comes into the hospital on the morning of the test. You will be given a sedative to help you relax and to make the baby lie still. A general anaesthetic is not necessary. A local anaesthetic is injected at the point where the fetoscope will enter, to "freeze" it. This means that there will be a sting when the local anaesthetic is given and momentary feeling of pressure when the fetoscope is put in, but otherwise you should feel no pain. The test takes about 20 minutes.

The fetoscope allows the doctor to see inside the womb, find the cord and draw a little blood for the laboratory tests.

After the test the woman rests for some time in hospital (hours in some places, one or two days in others).

The results of the blood test are available in * days. We telephone you with the result as soon as it comes. We know how worried you will be.

How do we test the baby's blood for thalassaemia major?

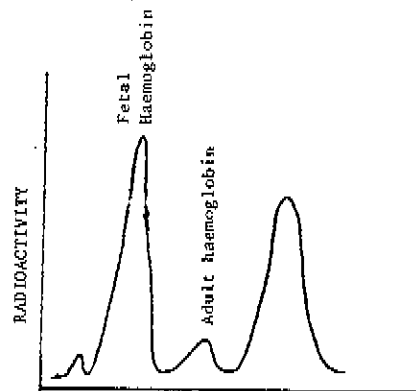
The test sorts out two different kinds of haemoglobin in the baby's blood. Adult haemoglobin (sometimes written HbA) and fetal or baby haemoglobin (sometimes written HbF).

A baby in the womb and for the first few months of life has mostly fetal (baby) haemoglobin. When it is about 6 months old the fetal haemoglobin goes and is replaced by adult haemoglobin. Thalassaemia is a disease of adult haemoglobin so a baby with thalassaemia major only shows signs of the disease after about 6 months of age.

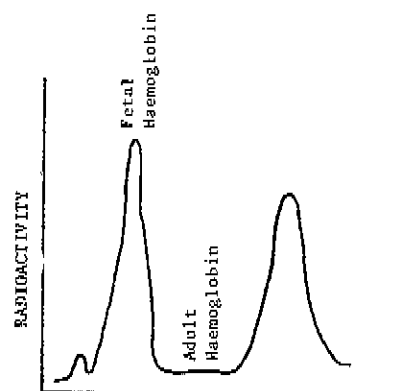
* Insert the appropriate figure.

In the womb, babies with normal blood make mainly fetal haemoglobin (HbF) but also a small amount (4-9%) of adult haemoglobin (HbA). Babies with thalassaemia trait make less adult haemoglobin (2-5%). And babies with thalassaemia major make even less, less than 2% of adult haemoglobin. So to find out if a baby in the womb has thalassaemia major we find out how much adult haemoglobin it has.

The test must be very accurate. The doctors first make the haemoglobin from the baby's blood radioactive. Then they use chemicals to separate the fetal haemoglobin from the adult haemoglobin in the baby's blood. They work out how much adult haemoglobin and how much fetal haemoglobin there is. Then they print out the results on a graph. The picture shows what it looks like.



Graph showing the haemoglobin in a baby with normal blood - a little Adult Haemoglobin



Graph showing the haemoglobin in a baby with thalassaemia major - almost no Adult Haemoglobin

You can see that even in a baby with normal blood, the amount of adult haemoglobin is very small. In a baby with thalassaemia trait it is half that much. In a baby with thalassaemia major there is little or no adult haemoglobin. If you have the test, we can show you your own graph.

Is the test reliable?

Sometimes the graph shows the baby's adult haemoglobin just between the level for thalassaemia trait and thalassaemia major. Then we do another test. The second time the result is always clear. We think the test is very reliable but in every medical test there is always a small possibility of a mistake. We think there is about a 1% chance of a mistake.

Is the test safe?

Every medical test carries a risk. In fetoscopy this is very small. There are practically no risks to the mother. Sometimes however the womb becomes very irritable after the procedure and contractions can start. Usually with treatment these contractions can be stopped. In about 1 in 50 cases however a miscarriage will occur. This happens mostly a few days after the test but occasionally a few weeks later.

To minimise these risks, for one to two weeks after the test the woman must take things easy, avoiding tiring housework and carrying heavy objects - e.g. shopping or children. Avoid sexual intercourse for ten days after the test. If any bleeding or discharge from the vagina occurs, contact the hospital immediately.

Is it possible for a baby to be diagnosed as healthy and yet to be found thalassaemic after it is born?

The laboratory tests are complicated but are carried out with the greatest possible care by an experienced team of scientists. However, there are pitfalls which can lead to a mistaken diagnosis and these have occurred all over the world. The risk for such an error is very small - less than 1% - but it does exist. If, as sometimes happens, the results are doubtful we may have to repeat the test two weeks later to get a clear result.

Termination of pregnancy

If the test shows that the baby has thalassaemia you may decide to end the pregnancy and try again later. The pregnancy is terminated by injecting special substances called prostaglandins into the womb. These stimulate contractions of the womb. In other words they bring on labour pains and start a miscarriage. The only other way to stop a pregnancy after 18 weeks is by an operation. But this will leave scars on your womb which can cause problems later.

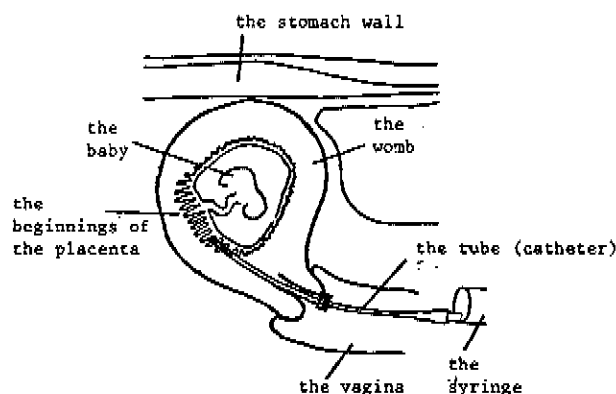
WHAT IS CHORIONIC VILLUS SAMPLING?

This test is called CVS for short. It is a new test that can be done very early in pregnancy, at about 9 weeks after your last menstrual period. We hope that this earlier test will be much less upsetting for you.

At present we cannot do this for everyone. We have to study blood beforehand from most members of the family to find out if we can do it for that particular family or not. It can usually be done if you already have a child who has thalassaemia major or normal blood. If you are having your first baby, or if your other children all have thalassaemia trait, we may not be able to do this early test for you. But if we can have blood from all four "grandparents" - that is the parents of both mother and father, we may still be able to do it. So we may ask for a lot of people to come to have their blood tested.

How do we do the test?

If you want your baby tested, you, the mother, come into hospital for a few hours one morning. Please bring your husband if he would like to come. We ask you to lie down and then we do an ultrasound scan to see exactly where the baby is. We can see more clearly if your bladder is full so we ask you to drink a lot of water before the test. We watch the test on the ultrasound all the time so we can see exactly what we are doing. We do not use a needle. Instead we put a very thin plastic tube into your vagina. The tube is so thin that most women hardly feel it. We want to take a very small sample of tissue from the edge of the placenta (where the baby is attached to you). We do not touch the baby, or the little bag of water it is lying in. The picture shows how the test is done.



The tissue test: the tube going into the womb

When we see by the ultrasound picture that the tube is in the right place we fix a syringe to the tube and gently suck some tissue out. We look at it under the microscope immediately to see if it is from the placenta. If it is, we can stop at once. If it is not, we put the tube back and try again. Sometimes we have to try 2, or even 3 times until we get tissue from the placenta. The test does not hurt at all and only takes about 10 to 15 minutes.

How do we test the tissue?

Your tissues are made up of lots of tiny cells. The most important part of each cell is called the nucleus. Each nucleus contains a substance called DNA which shows all the characteristics you have inherited from your parents, such as your eye and hair colour, the shape of your nose, and what kind of haemoglobin you have.

Now scientists can take the baby's DNA out of the tissue we take from the placenta and find the part of the DNA which shows what kind of haemoglobin a person has. To find out if your baby has thalassaemia major, they first look at DNA from the blood samples we have taken from you, your husband and your other children. Then they compare it with DNA from the baby's tissue. It takes about 2 weeks to do the comparison. We tell you the results as soon as we know.

If your baby has thalassaemia major you may decide to terminate the pregnancy.

How do we terminate the pregnancy?

Termination is quite quick and painless if you are less than 14 weeks pregnant. You come into hospital one evening. The next day you are put to sleep as if you were having an operation. Your womb is emptied through your vagina. The operation is quick and you will feel no pain. You can go home the next day. The termination does not spoil your chance of having another baby.

Is the tissue test accurate?

We think the test is very accurate but the methods used in the laboratory are still very new. In every medical test there is a small possibility of a mistake. Possibly nature itself can "play a trick" and make us make a mistake. Occasionally all human beings make a mistake however careful they try to be. We think there is a small (1-2%) chance of making a mistake with this test.

Is it safe?

We are still not sure how safe the test is. The main risk is that we could cause a miscarriage. The test is as gentle as possible but anything that interferes with a pregnancy may cause a miscarriage. We think that the risk with this test is about 3% but it is difficult to tell because about 1 in 10 pregnancies miscarries anyway before 12 weeks. We are doing some special studies to try to find out more about the exact risk.

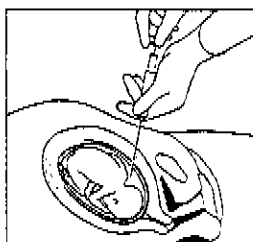
WHAT IS AMNIOCENTESIS?

This test is done at about 17 weeks of pregnancy, but it is easier and a bit safer than fetoscopy. It can be done for most - but not all - mothers who could have a child with thalassaemia major. In fact, it can be done for the same mothers who could have the chorionic villus sampling test (see page 3.5).

However, sometime we see these mothers for the first time when their pregnancy is too far on for them to have the early test. Then we offer them amniocentesis because it is a bit safer than fetoscopy.

Amniocentesis is done at about 17 weeks after the last menstrual period. The doctors put a small needle into the womb and take out a small amount of the fluid around the baby.

Amniocentesis



The mother is asked to come to the hospital for an ultrasound scan some days before the test, or even on the day of the test. No sedative tablets or local anaesthetic is necessary. There is only a momentary feeling of pressure when the needle is put in. It usually takes only a few minutes to draw off some fluid.

The results of this test take about 2 weeks to come from the laboratory.

Is amniocentesis safe?

As we said before, every medical test carries a risk, but the risk of this one is very small. It is almost entirely safe for the mother, and there is less than a 1 in 100 chance that it could cause a miscarriage.

Is it accurate?

It is just as accurate as the CVS test (see page 3.5).

Termination of pregnancy

If the test shows that the baby is thalassaemic, you may decide to end the pregnancy. This is done in the way described on page 3.5.

PLEASE COME EARLY

Because we don't want to do the tests in a rush we like to test your blood before you get pregnant, if we can. If you are planning to have another baby and think you will want to have it tested for thalassaemia major, please come in for a blood test soon. We will need to take small blood samples from you, your husband and any other children who have normal blood or thalassaemia major. If you are already pregnant and want the baby tested, contact the doctors who are involved in this kind of work. They will be able to answer your questions accurately, and will arrange for you to have a test - if you want one. To find out where your local centre is ask your family doctor or contact the Thalassaemia Society. Their address is at the end of this booklet.

What should you do now?

If your partner has not been tested for thalassaemia trait ask him or her to go for a blood test.

Show this booklet to other members of your family too - your cousins, neices, nephews, etc. If they haven't already had a blood test, encourage them to go for one also.

If you and your partner both carry thalassaemia trait you should ask your G.P. to arrange a visit to a genetic counsellor to find out about ways to avoid having children with thalassaemia major. You should see the genetic counsellor as soon as you think a pregnancy has started. If you have any difficulty, contact the Thalassaemia Society.

Take this booklet with you if you or your partner go to the doctor to arrange a blood test, or for any other advice about your thalassaemia trait.

For more information about thalassaemia trait either 'phone or write to:

*

We thank Alix Henley, and Rosie Leyden of the UK Health Education Council, for help and advice in preparing this booklet.

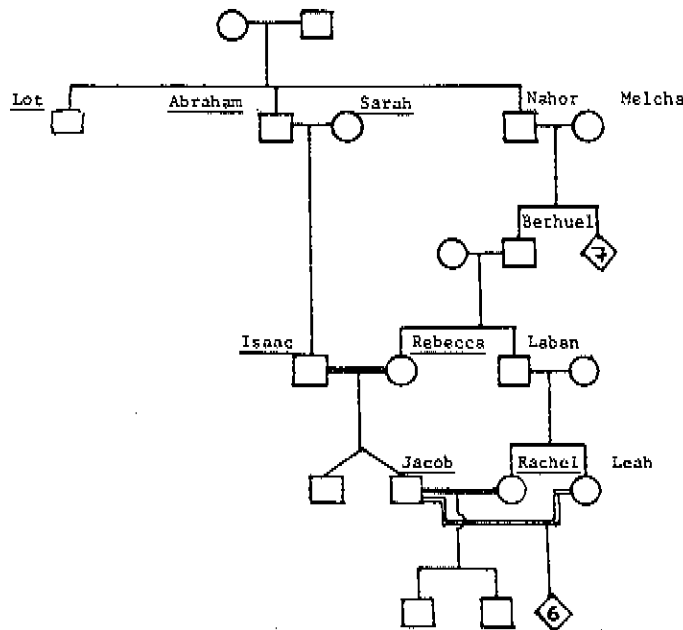
*Put the appropriate contact address and phone number here.

MARRYING A CLOSE RELATIVE - IS IT A MEDICAL PROBLEM?


A leaflet for those who may consider marrying a close relative


In certain societies and communities there are mistaken ideas and beliefs about the medical consequences of marrying a close relative. There are also very different customs in different countries, concerning marriage to relatives. In some, such marriages are encouraged, while in others they may be forbidden. The purpose of this leaflet is to explain some medical points about which you may have questions, worries or concerns.

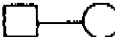
This is a booklet about families and relatives, so it is best to start by showing you how to draw a family tree. A well-known family tree is shown in the picture.



Family tree of the Patriarchs Abraham, Isaac and Jacob


The men and boys are shown by squares 

The women and girls are shown by circles 


A married couple are connected by a single straight line 


A married couple of close relatives is shown by a double line

Their children are shown below the couple, as if they are on a hanger, arranged in order of birth with the oldest on the left


A pregnancy at the time of drawing is shown as a small circle 

Someone who has died is shown by a line through the square or circle --

Dead woman or girl 

Dead man or boy 

The name and year of birth may be put beside each circle or square.

A number of children may be shown by a diamond, with the number inside. 

Perhaps you would like to draw your own family tree here. If you are going to consult a Clinical Geneticist, it is a good idea to draw your family here together with the geneticist, so that you can keep a permanent record of it.

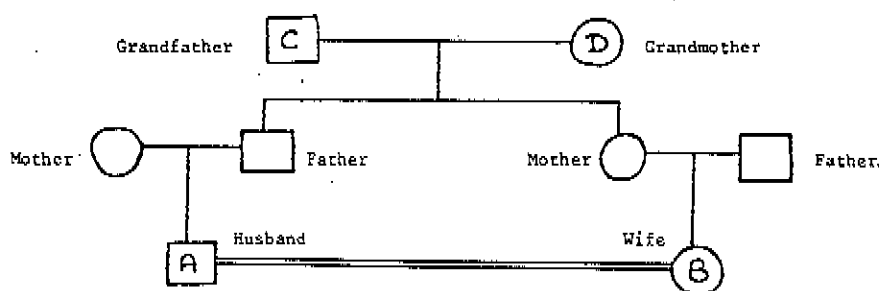
NAME OF FAMILY:

DATE OF DRAWING:

A marriage between close relatives is called a "consanguineous marriage". Consanguineous is a Latin word meaning the couple have "similar blood".

Who is a close relative?

People who have a grandparent or great grand-parent in common, as in this picture are close relatives.



A and B are first cousins. They are close relatives (consanguineous) because they have the same grandfather (C) and grandmother (D). Men are shown by squares , and women are shown by circles .

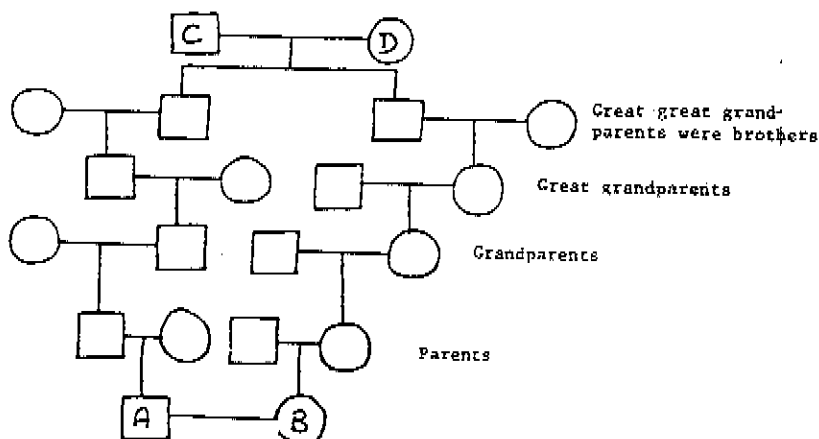
This "common ancestor" can be from your mother's side or from your father's side. All first cousins are "close relatives". They include any of the following:

- * The son or daughter of your father's brother
- * The son or daughter of your father's sister
- * The son or daughter of your mother's brother
- * The son or daughter of your mother's sister

Uncles (your father's brother, your mother's brother) and nieces are also very close relatives.

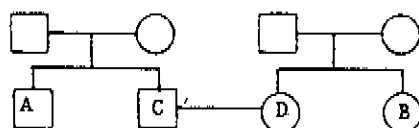
Who is not a close relative?

If your common ancestor was many generations back, as in this picture, your relative is called a "far relative"



A and B are "far relatives" because the common ancestors C and D are many generations back. If they marry, this is not considered a consanguineous marriage.

Your in-laws and their family members are not "close relatives" if you and they do not have a common ancestor, as in this picture.



C and D are married, but A (the brother of C) and B (the sister of D) are not close relatives because they do not have a common ancestor. They are in-laws. If A and B marry this is not a consanguineous marriage.

In a marriage with a close relative, is there necessarily a risk of having children with an inherited disease

Certainly not. Marrying a close relative does not necessarily cause illness in children.

Some people think (wrongly) that a marriage with a close relative must lead to the birth of children who are malformed or who have serious inherited diseases. Specialists in inherited diseases have studied consanguineous marriages. Their studies show that in most cases such marriages do not have any serious medical consequences. However, occasionally they may lead to the birth of children with an inherited disease.

Only one type of inherited disease occurs more commonly in consanguineous marriages. These are called "autosomal recessive diseases", "recessive diseases" for short. The following paragraphs will explain which particular situations can lead to the birth of sick children, and will also explain how you can avoid these inherited diseases. But first we must talk a little about inheritance, that is, about how parents pass their characteristics on to their children. The following description is true only for recessive diseases.

WHAT IS AN INHERITED DISEASE?

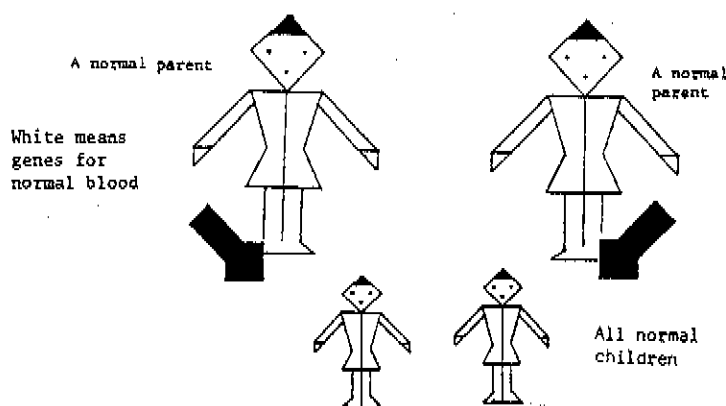
All of us inherit a lot of characteristics from our parents. For example, your hair and skin colour, the shape of your nose, the kind of haemoglobin you have in your blood. Your body is built up from a lot of "cells" that are too small to see. In every cell you have a pair of "genes" (inherited material) for every characteristic you inherit. One of each pair of genes comes from your mother (through the egg) and one from your father (through the sperm). Similarly, when you yourself make eggs or sperm, each egg or sperm contains only one of each pair of the genes that you inherited from your parents. So you will pass some of your parents' genes on to your children.

Most of the genes you receive from your parents and pass on are healthy, but a few are defective. If only one of your two genes for a particular characteristic is defective, you are usually completely healthy, because the other gene works normally, it "compensates" for the defective gene. Such a defective gene is called a recessive gene because it "hides behind" the normal one. Examples of diseases carried by recessive genes are thalassaemia, sickle cell anaemia, cystic fibrosis. We leave a space here for the doctor to add any that could be particularly important for you

A person who has one recessive gene paired with a normal gene is called a "healthy carrier" ("carrier" for short) of thalassaemia, sickle cell anaemia or cystic fibrosis.

We will use thalassaemia as an example to show how these genes are passed on in families, and how they can sometimes lead to the birth of sick children.

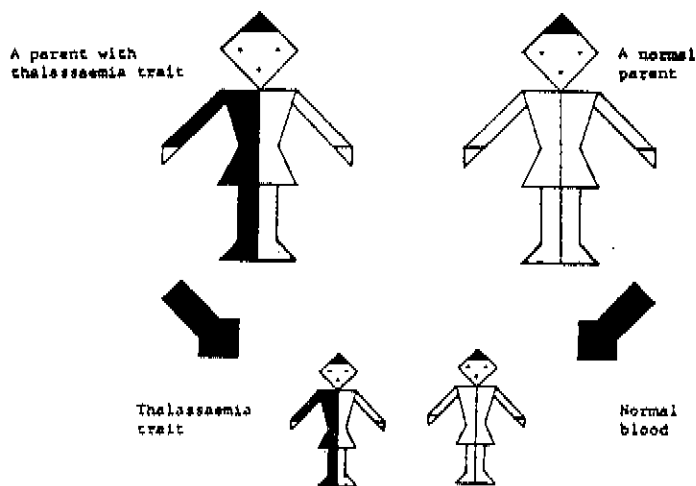
In thalassaemia one of the special genes that control the haemoglobin in the red blood cells is defective. Haemoglobin is what makes blood red; it carries oxygen to all the parts of the body. The first example shows two people who do not carry a thalassaemia gene. If they have children they cannot possibly hand on thalassaemia. All their children will have normal blood.



In many countries quite a lot of people are carriers of thalassaemia. They are healthy because they have inherited one gene for thalassaemia from one parent, and one normal gene from the other. The normal gene protects them so they are quite well and usually do not have any idea that they are "carriers". The thalassaemia gene alters their blood slightly (it

makes the red blood cells a bit smaller), so special blood tests can show if you are a thalassaemia carrier or not. People who carry thalassaemia are said to have "thalassaemia trait", because it causes such very small changes.

When they have children, the thalassaemia carrier can pass on either a thalassaemia gene, or a normal gene, to each child. Their partner always passes on one of their two normal genes. So there is a 1 in 2 (50%) chance that each of their children will have thalassaemia trait, and a 1 in 2 (50%) chance that they will not. One thalassaemia gene cannot do any harm, so none of their children can have thalassaemia major, the disease.



White stands for normal genes, the black stands for the thalassaemia gene.

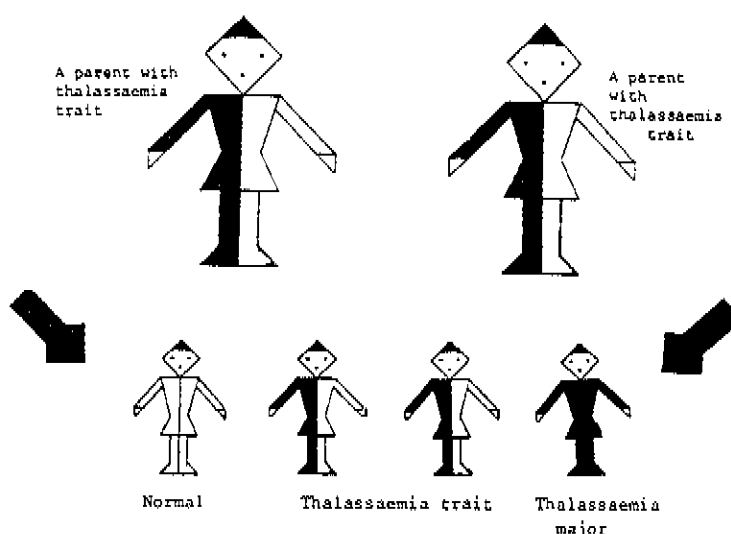
Thalassaemia carriers are completely healthy, so thalassaemia can be passed on through many generations and nobody will realise that it is "in the family" unless they have special blood tests to find out if anyone is a carrier.

In fact, very many families are passing on one or another type of inherited disease in this way. Carriers of some of these other conditions can also be detected by blood tests in the same way as thalassaemia carriers, but many cannot.

The only danger in being a thalassaemia carrier, is that if by chance you marry another carrier, you may both pass your defective gene on to some of your children. Some of your children could have an inherited disease. The picture shows how this can happen.

When both parents carry thalassaemia some of their children may inherit the normal gene from one of them and the thalassaemia gene from the other. They will have thalassaemia

trait. Some may even inherit the normal gene from both parents and will therefore have completely normal blood. But some may inherit a thalassaemia gene from both parents. These children will have thalassaemia major.



The white stands for a normal gene, and the black for a thalassaemia gene.

If both parents have thalassaemia trait, in each pregnancy there is a 1 in 4 (25%) chance that their child will have normal blood, a 2 in 4 (50%) chance that the child will have thalassaemia trait (like the parents) and a 1 in 4 (25%) chance that the child will have thalassaemia major. Put another way, this means that there is a 3 out of 4 (75%) chance that a future child will not have thalassaemia major.

There are several ways for married couples who know they are both thalassaemia carriers to avoid having children with thalassaemia major.

For instance, there is a special test that can be done in each pregnancy at about 8 weeks from the beginning, to see if that particular fetus has thalassaemia major or not. If it does not, the parents can continue the pregnancy in confidence. If it does, they can decide whether to stop that pregnancy early on and try again, or to continue it knowing that the child will need special medical treatment. Many couples of carriers do decide that it is not right to continue the pregnancy when they know that the child will be ill.

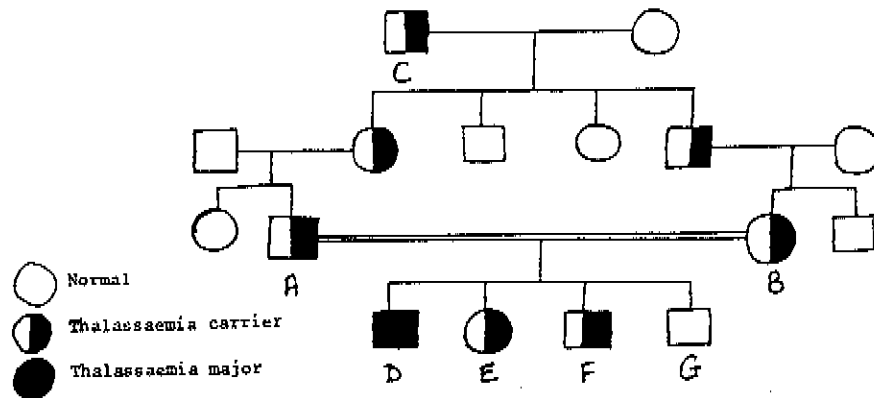
HOW CAN CONSANGUINEOUS MARRIAGE LEAD TO INHERITED DISEASES?

Thalassaemia is only one example of an inherited disease. There are in fact several thousand different rare inherited diseases. Some, but by no means all, are inherited in the "recessive" way described here, and it is only this type of inherited disease that is specially important for people who may marry a close relative.

The carriers of some of these rare recessive diseases can be detected by special blood tests, and some cannot.

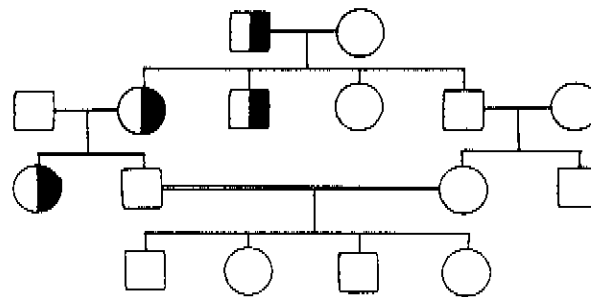
Each one of us carries many different types of rare defective genes. The defective genes that you carry are usually different from those your partner carries. So it is very unlikely that two defective genes of the same type can come together in your child to produce a

disease. On the other hand if you and your husband or wife are close relatives, there is a chance that you might both have inherited the same defective gene from a common ancestor and could both pass it on to your child. The picture shows how this can happen.



A and B are first cousins. They both carry the same defective gene which they have each inherited from their grandfather C. Even though they are both healthy, on average 1 in 4 of their children will inherit both defective genes, and suffer from an inherited disease.

But even if there is an inherited disease in the family, this does not necessarily mean that cousins who marry will both be carriers. The picture also shows that this need not happen. In fact, the chance that two cousins will both carry the same defective gene is only about 1 in 8 (12.5%): though it may be higher if there have been many cousin marriages within the family.



WHEN DOES MARRIAGE WITH A CLOSE RELATIVE HAVE NO SERIOUS MEDICAL CONSEQUENCES?

If there is no known inherited disease in your family on your side, on the side of your close relative, or in a common ancestor, then there is very little extra risk that you will have a child with an inherited disease if you marry a close relative. Even if there is an inherited disease in the family, there is usually only an extra risk in marrying a close relative if the disease is inherited in the recessive way described here.

WHEN DOES MARRIAGE WITH A CLOSE RELATIVE REQUIRE MORE CAREFUL CONSIDERATION?

If you know that someone in your family on your side or on the side of your proposed partner, has had one or more children with a serious lifelong illness starting early in life, there is a possibility that there is a recessively inherited disease in the family. If this is so, there is an increased risk that you could have children with the same disease if you marry a close relative.

WHAT CAN YOU DO TO FIND OUT IF YOU HAVE AN INCREASED RISK?

Ask your doctor to send you to see a specialist in inherited diseases, a clinical geneticist.

HOW CAN A CLINICAL GENETICIST HELP?

Firstly, he or she can help you to know if there really is an inherited disease in your family. Most often in discussing together you will find that there is no reason to think that some diseases of some family members are inherited. So the visit may reduce any worries or anxieties you may feel.

Secondly, if there really is an inherited disease in your family, the geneticist may be able to explain it exactly to you, including how severe it is, what treatment is possible, and whether carriers can be detected by special tests. The doctor will be able to tell you what your risk of having a child with the same disease is, if you marry your close relative.

Thirdly, there are special tests for carriers of many inherited diseases, so it may be possible to find out whether or not you carry one of the common inherited diseases like thalassaemia, or an inherited disease which is present in your family. It is worth having the test if one is available, because you may find that neither you nor the close relative you plan to marry is a carrier. If this is so, then you could not possibly have a child with that disease.

Even if one of you carries the defective gene and the other partner does not carry it, there is no fear at all of having affected children. Some of these tests are rather difficult to do for pregnant women, so it is wise to ask for a blood test before you become pregnant.

WHAT CAN YOU DO IF BOTH PARTNERS ARE CARRIERS OF THE SAME DEFECTIVE GENE?

You only need to worry about having affected children if both partners carry the defective gene. Then there is a 1 in 4 chance in every pregnancy of having a child affected with the disease, as we have already seen. In such situations special tests can be done early in pregnancy to see if the fetus is affected with the disease or not. Most often, of course, you would find that the fetus is not affected, so you can continue the pregnancy with confidence. However, if the fetus is affected you may decide to ask for that pregnancy to be terminated, and to try again to conceive a normal child. The choice of whether to have the test, and whether you continue or terminate an affected pregnancy, are always yours.

Finally, always remember that even when both husband and wife carry the same defective gene, there is a three-quarters (75%) of having a normal baby unaffected by the disease in each pregnancy.

HOW CAN YOU GET FURTHER INFORMATION ABOUT THIS SUBJECT?

If you have any questions about a particular problem or concern in your own family about these subjects, ask your doctor to arrange a visit to a specialist clinical geneticist.

You are welcome to contact us directly yourself at the following address:*

*give appropriate contact address.

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