Carrying Beta Thalassaemia

A carrier can use this booklet to…

- *help explain carrying beta thalassaemia to their partner, blood relatives and others.*
- *show to any health professional (doctor, nurse or midwife) they see about having a family , or pregnancy, or carrying beta thalassaemia.*

Contents

Introduction

Beta thalassaemia is one of a range of variations in the blood called *haemoglobin gene variants*. Here we call them *haemoglobin variants* for short.

Carriers of beta thalassaemia are also sometimes said to to *have beta thalassaemia trait*, or to *have beta thalassaemia minor*.

Beta thalassaemia is inherited. That is, it is passed on from parents to their children, like height, hair colour or eye colour. It is passed on equally by men and women. It is present at birth, and it remains the same for life.

It is important to distinguish clearly between people who *carry beta thalassaemia* and people who *have a haemoglobin disorder*.

Carriers of beta thalassaemia…

… inherited beta thalassaemia from one of their parents. Carrying beta thalassaemia does not affect their own health. However, if their partner is also a carrier they could have children with a haemoglobin disorder.

People who have a haemoglobin disorder…

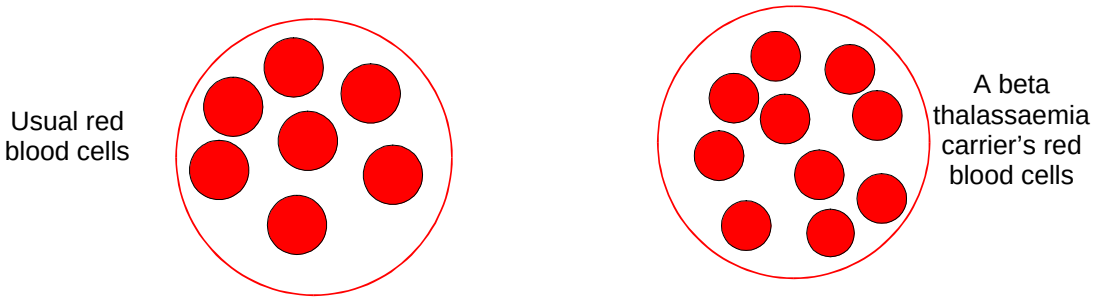
… inherited two haemoglobin variants, one from each of their parents. Together, the two variants cause a serious inherited anaemia that can lead to life-long health problems.

This document is about carrying beta thalassaemia.

What does it mean to carry beta thalassaemia?

Blood is made up of millions of *red blood cells* floating in a fluid called *plasma*. Red blood cells are full of haemoglobin, which is red. This is why blood is red. The heart pumps blood round the body through the blood vessels. The body needs oxygen to function. Haemoglobin picks up oxygen as blood passes through the lungs, and carries it to the rest of the body as the blood circulates.

Carriers of beta thalassaemia have smaller red blood cells, but more of them than other people. You can see the difference between other peoples' red blood cells and a thalassaemia carrier's red blood cells by looking down a microscope.



Beta thalassaemia is *inherited* - it is handed on from parents to their children, it is present at birth, and it remains the same for life.

How is beta thalassaemia inherited?

It is inherited through *genes.* Every human characteristic, such as eye colour, or height, or type of haemoglobin is controlled by genes that parents pass on to their children. A child inherits two genes for every characteristic, one from each parent. Most people inherit two genes for the usual type of haemoglobin, *haemoglobin A.* Each gene is responsible for making half of the haemoglobin A in each red blood cell.

A carrier of beta thalassaemia has inherited a gene for haemoglobin A from one parent and a gene for beta thalassaemia from the other. The beta thalassaemia gene can make only a small amount of haemoglobin, or none at all. As a result people who carry beta thalassaemia have red blood cells that contain less haemoglobin than usual, and so are smaller than usual. They make up for this by making more red blood cells. Their blood functions normally, and carrying beta thalassaemia does not cause them any health problems.

How do people find out that they carry beta thalassaemia?

By having a special blood test "for haemoglobin disorders". This usually involves two steps.

- The first step is to measure the size of their red blood cells. This shows that they have smaller red blood cells than usual.
- The second step is to analyse the types of haemoglobin in their blood. Most adults have haemoglobin A with a small amount of a slightly different haemoglobin called haemoglobin A_2. Usually blood contains less than 3% of haemoglobin A_2. Beta thalassaemia carriers have 3.5 - 6% of haemoglobin A_2.

Can carrying beta thalassaemia affect your health?

Carriers of beta thalassaemia are not ill, and are no more likely to get ill than other people. Carrying beta thalassaemia does not make them weak, and they can do any kind of work they choose.

Some carriers have a mild anaemia. Anaemia means having a lower haemoglobin level than usual. Anaemia due to carrying thalassaemia has no effect on health or length of life.

The commonest type of anaemia is iron deficiency anaemia. It occurs in people whose diet contains too little iron, or who lose blood for some reason. People with iron deficiency anaemia may also have small red blood cells.

Occasionally a doctor thinks a person who carries thalassaemia must be short of iron because they have small red blood cells. If the doctor prescribes iron medicine, in the long run this could do more harm than good. A carrier should take iron medicine only if a special blood test (serum iron or serum ferritin) shows that they are short of iron.

Can a carrier of beta thalassaemia also get iron deficiency anaemia?

They can. They should have a diet with enough vitamins and iron to make sure that this does not occur.

What about pregnant women?

Like other pregnant women, women who carry thalassaemia can become iron deficient and may need extra iron.

Anaemia due to carrying thalassaemia can become more severe during pregnancy, and sometimes a pregnant carrier can need a blood transfusion. The anaemia gets better after the baby is born.

Is there any treatment to get rid of beta thalassaemia?

No, a person who is born carrying beta thalassaemia will always carry it.

Can carrying beta thalassaemia turn into a serious form of thalassaemia?

It cannot.

Can people catch beta thalassaemia from a carrier?

They cannot.

Can a carrier of beta thalassaemia be a blood donor?

They can give blood like other people, provided they are not anaemic.

The blood transfusion service tests donors for anaemia before each blood donation. This test will exclude a thalassaemia carrier with mild anaemia.

Is it a bad thing to carry beta thalassaemia?

It is not. Carriers of beta thalassaemia are healthier than other people in several ways. For example, they have some natural protection against severe forms of malaria.

Malaria parasites live inside red blood cells, and are most comfortable in the red cells of people who do not carry any haemoglobin variant. Thalassaemia carriers can be infected with malaria like anyone else, but the parasites cannot grow well in their small red blood cells. Therefore they have less severe infections and less chance of dying from malaria than other people.

In countries where it was common malaria used to kill many children. Children who carried thalassaemia survived better than other children and passed thalassaemia on to their children in turn. As time passed carrying thalassaemia became very common in such areas, and that is why there are now so many carriers in the world.

Malaria has been eradicated in many countries, so being a carrier is less advantageous than it used to be. Thalassaemia does not go away when malaria is eradicated, or when a carrier moves to a different part of the world, because it is inherited.

Carriers of beta thalassaemia should not rely on their natural protection against malaria when they visit a malarious country. Their protection is limited. They should take antimalarial tablets like everybody else.

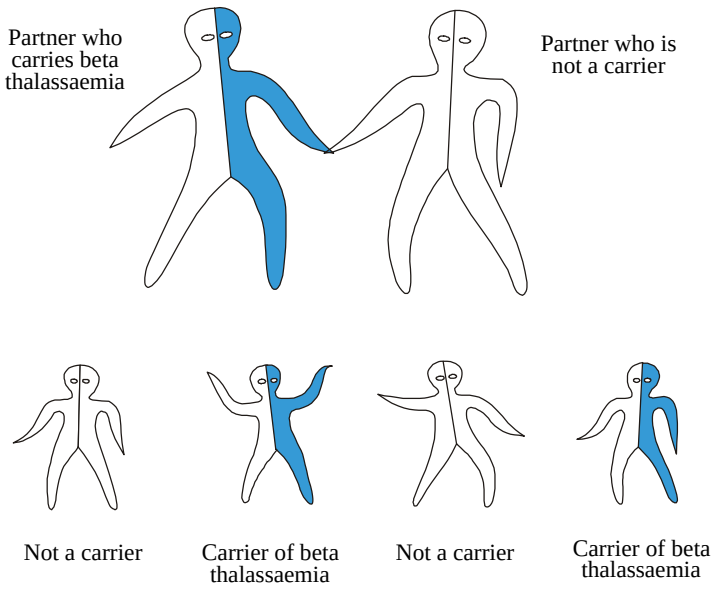
Does carrying beta thalassaemia have any other health advantage?

Recent research shows that beta thalassaemia carriers are less likely than others to suffer from heart attacks. In the modern world, this is an important advantage.

Carriers have a limited natural protection against heart disease. To benefit from it they also need to adopt a healthy life-style, with no smoking, adequate exercise and a balanced diet.

Implications for a carrier's children…

If one partner carries beta thalassaemia and the other does not carry any haemoglobin variant, their children could not have a serious haemoglobin disorder



In each pregnancy, there are two possibilities.

- The child may not carry any haemoglobin variant.
- The child may carry beta thalassaemia. This is harmless.

This couple has the same chance of a healthy family as other couples do.

There is also no risk of a serious haemoglobin disorder if one partner carries beta thalassaemia and the other carries any of the following:

alpha thalassaemia

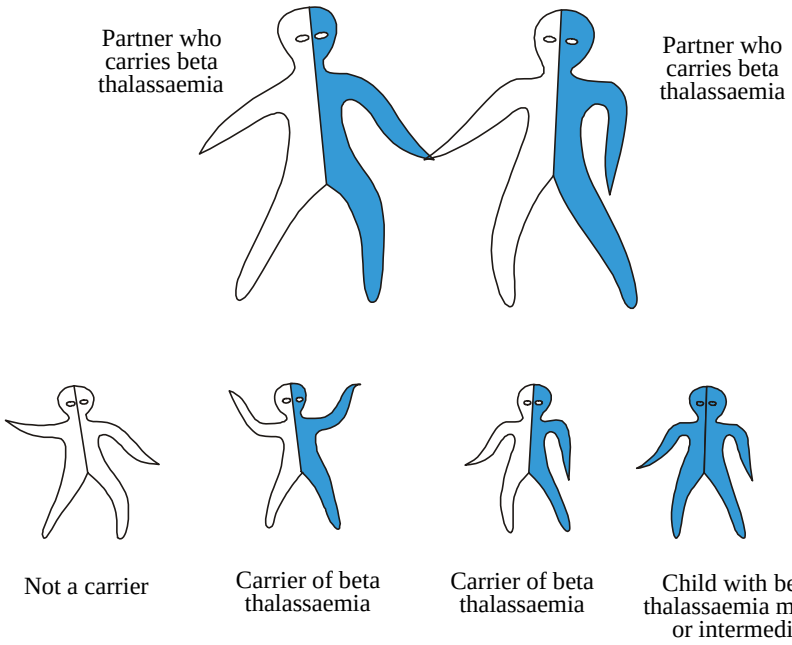
haemoglobin C

haemoglobin D

hereditary persistence of fetal haemoglobin (HPFH)

one of a range of possible rare haemoglobin variants

If both partners carry beta thalassaemia, their children could have homozygous beta thalassaemia (beta thalassaemia major or intermedia)



In each pregnancy, there are three possibilities.

- The child may not carry any haemoglobin variant.
- The child may carry beta thalassaemia. This is harmless.
- The child may inherit beta thalassaemia from both parents. This child would have honozygous beta thalassaemia.

In each pregnancy there is a 3 in 4 chance of a healthy child and a 1 in 4 risk of a child with honozygous beta thalassaemia.

There is also a known risk of a serious haemoglobin disorder when one partner carries beta thalassaemia and the other carries any of the following:

delta-beta thalassaemia

haemoglobin E

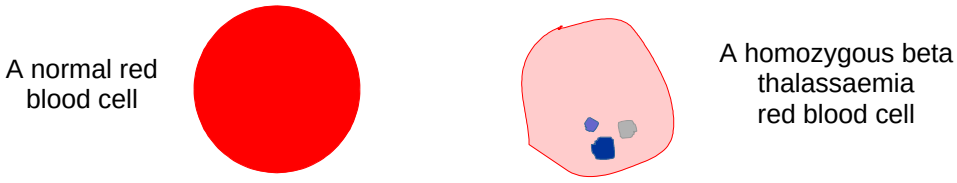
haemoglobin Lepore

haemoglobin S

one of a few rare haemoglobin variants

What is homozygous beta thalassaemia?

People with homozygous beta thalassaemia cannot make haemoglobin normally, and so cannot make normal red blood cells. Each red blood cell contains much less haemoglobin than usual, and there are far fewer of them than usual. This causes a serious anaemia. More than nine out of ten such people have *beta thalassaemia major*.



A child with beta thalassaemia major is normal at birth but develops a severe anaemia between three months and one year of age. If left untreated affected children have a miserable life and most die before five years of age.

About one in ten people with homozygous beta thalassaemia have *beta thalassaemia intermedia* - they have a serious anaemia but can manage without regular blood transfusions in the early years of life. The anaemia often gets worse with age, and many start to need regular blood transfusions later in childhood or in adult life.

About one in a hundred have *mild beta thalassaemia intermedia* - they have some anaemia but can lead a practically normal life with very little medical treatment.

What is the treatment for beta thalassaemia major?

The basic treatment is regular blood transfusion, usually every four weeks. Children who are transfused appropriately grow well and have a normal life. However, to live past their twenties they also need treatment to remove iron.

After each transfusion, the transfused red blood cells break down slowly and release iron. This builds up in the body and causes iron overload, which can ultimately damage the heart, liver, and other organs. Iron can be removed by drugs called *iron chelating agents* that bring it out in the urine. The traditional iron chelating agent, *desferrioxamine*, is injected under the skin during most nights using a small pump.

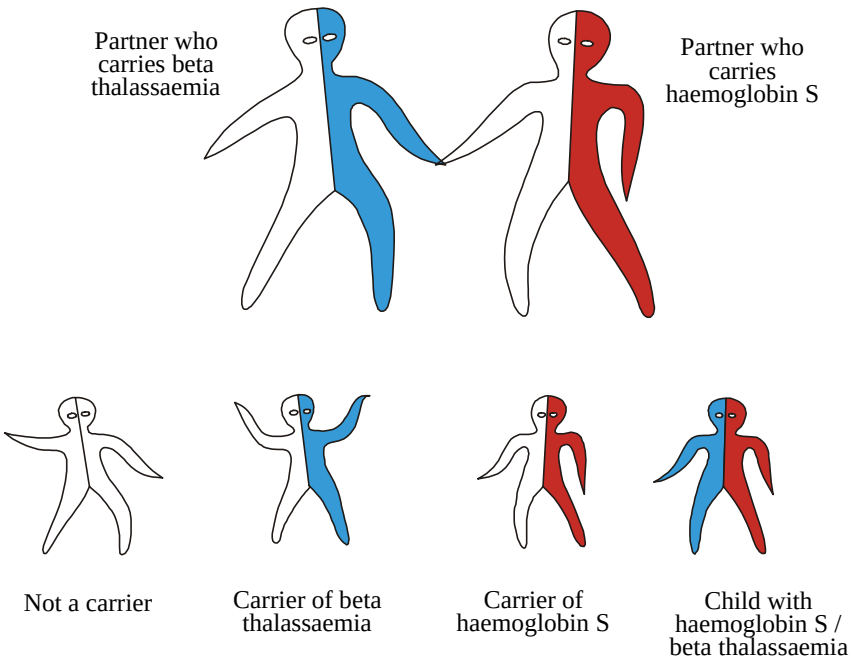
A child born today with beta thalassaemia major is expected to live an almost normal length of life, provided that they can obtain all the treatment they need, and take it regularly. However, the present treatment for iron overload is extremely burdensome and some patients find it intolerable. Iron overload is still the main cause of death in thalassaemia major today.

The outlook is steadily improving. A new iron chelating agent that can be taken by mouth is increasingly available. In addition, when a compatible related donor can be found, some patients can be “cured” by bone marrow transplantation.

Is it possible to predict how severe homozygous beta thalassaemia might be?

DNA tests can help to predict if a couple who both carry beta thalassaemia could have children with beta thalassaemia major or beta thalassaemia intermedia.

If one partner carries beta thalassaemia and the other carries haemoglobin S, their children could have haemoglobin S/beta thalassaemia



In each pregnancy, there are four possibilities.

- The child may not carry any haemoglobin variant.
- The child may carry beta thalassaemia. This is harmless.
- The child may carry haemoglobin S. This is harmless.
- The child may inherit beta thalassaemia from one parent and haemoglobin S from the other. This child would have haemoglobin S/beta thalassaemia.

In each pregnancy there is a 3 in 4 chance of a healthy child and a 1 in 4 risk of a child with haemoglobin S/beta thalassaemia.

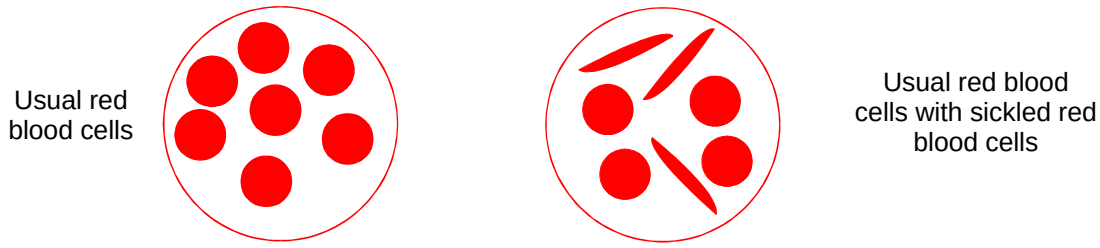
What is haemoglobin S/beta thalassaemia?

It is a *sickle cell disorder*. Sickle cell disorders can cause anaemia, infections, chest problems and painful crises. A painful crisis is an unpredictable attack of very severe pain, that can occur anywhere in the body. The hands and feet are often affected in young children, the limbs and back in adults.

Some people with haemoglobin S/beta thalassaemia have very few medical problems. Many have two or three infections or painful crises a year, and may need to be admitted to hospital from time to time. A few have frequent severe problems and may need regular blood transfusions to avoid organ damage. There is an increased risk of premature death, even for people with few other problems.

What causes haemoglobin S/beta thalassaemia?

When a person has one gene for beta thalassaemia and one gene for haemoglobin S, they cannot make haemoglobin A normally, and their red blood cells contain mainly haemoglobin S. This is called *sickle cell haemoglobin* because it causes red blood cells to change from their normal disk-like shape to a sickle shape (long, curved and pointed), when they are short of oxygen. Sickled red blood cells can become jammed in small blood vessels, block the blood supply, and cause pain in that part of the body.



What is the treatment for sickle cell disorders?

People with a sickle cell disorder, and their family, need to understand the condition so that they can take steps to avoid problems as far as possible. For example they can reduce the risk of painful crises by drinking plenty of fluid and avoiding extremes of heat and cold. They should take penicillin daily to reduce the risk of infections, and their diet should contain adequate vitamins. They should attend a sickle cell clinic regularly so that problems can be detected and treated as early as possible.

They can have a wide range of other problems each requiring different, appropriate treatment.

Is it possible to predict how severe haemoglobin S/beta thalassaemia would be?

Its severity partly depends on the type of beta thalassaemia gene involved. When combined with haemoglobin S, types of beta thalassaemia that are common among people of Mediterranean origin often cause a severe disorder. Types that are common among people of African origin often cause a mild disorder. Therefore the partner who carries beta thalassaemia should have a DNA test to find out the exact type of beta thalassaemia they carry.

Can serious haemoglobin disorders be prevented?

Carrier couples who know of the risk for their children have a number of choices. They can take steps to make sure that they have healthy children, and can make sure that affected children have the best possible care from birth. Their choices are not simple. They need to know their risk early, so that they have enough time to make the decisions that are right for them.

In the UK, it is national policy to identify and inform as many carriers as possible before they have children, so that they can have an informed choice. The NHS is expected to take the following steps.

- *Offer carrier testing*. At present this is usually offered by midwives to pregnant women. In some districts it is offered to all pregnant women, and in others only to pregnant women with ancestors from areas where haemoglobin variants are common.
- *Inform carriers.* They need information on (a) the possible risk to the health of their children, and (b) the need for their partner to have a carrier test.
- *Inform carrier couples*. Couples who are both carriers need to see a specialist counsellor for haemoglobin disorders. The counsellor will find out whether they are "at risk" for having children with a serious haemoglobin disorder, and inform them of the exact nature of the risk and the possibilities for avoiding it.

All at risk couples should be offered both *prenatal diagnosis* and *neonatal diagnosis* (new-born diagnosis).

- Prenatal diagnosis means testing an unborn baby to see whether it has a serious disorder. DNA tests are done on a tiny amount of tissue taken from the developing placenta. This can be done as early as 11 weeks of pregnancy. If the baby is affected, the parents can decide whether to continue the pregnancy and plan the best possible care for the baby, or to terminate the pregnancy and try again for a healthy child.
- Neonatal diagnosis is done after the baby is born, using blood taken from the umbilical cord or by pricking the baby's heel a few days after birth. Neonatal diagnosis for thalassaemia is done by DNA tests. When there is a risk of a sickle cell disorder, early diagnosis and treatment can be life-saving for the child.

It is now recognised that screening during pregnancy often identifies at risk couples too late. Carrier testing should be offered by family doctors either before pregnancy, or as soon as a pregnancy has started.

Asking a partner to have a blood test

A carrier who is thinking of having children needs to tell their partner that they carry beta thalassaemia, and ask him or her to have a blood test “for haemoglobin disorders”.

Is it difficult for a carrier to ask their partner to have a blood test?

It can be easy in some cases and difficult in others. It is easier if both the carrier and their partner know that:

- Carrying a haemoglobin variant is common.
- The test will probably show that the partner does not carry a haemoglobin variant.
- If they do carry a haemoglobin variant it will not affect their health or lifestyle in any way.
- A couple who are both carriers can have a healthy family, with medical help.
- Expert counselling is available.
- No-one will try to tell the couple what to do: all the choices are theirs.
- The results of blood tests, and the couples’ decisions, are completely confidential.

If a couple are both carriers, can it interfere with their relationship?

It is unusual for a relationship to suffer because one or both of a couple carry a haemoglobin variant. On the contrary, many couples draw closer together to deal with their problem. This is true whether they are just starting their relationship or have been together for a long time.

When is the best time for a carrier to ask their partner to have a blood test?

Ideally as early as possible, because it can take time to arrange a blood test, and a couple who are both carriers need time to decide what to do. Of course, the best timing depends on the couple’s relationship with each other. It may also be influenced by their families’ views, and the culture they belong to.

In practice a carrier might suggest a blood test to their partner at one of the following points.

- Before they settle down together.
- After they settle down together but before they start a pregnancy.
- As soon as they have started a pregnancy.

Telling the family about beta thalassaemia

A carrier inherited beta thalassaemia from one of their parents, so their brothers and sisters and other blood relatives could also be carriers. For example a brother or sister has a 1 in 2 chance of being a carrier.

If a carrier has brothers or sisters, or already has children, they need to know that they may carry beta thalassaemia. They should ask their GP or practice nurse for a blood test “for haemoglobin disorders”.

Beta thalassaemia world-wide

- Beta thalassaemia major is one of the commonest serious inherited disorders.
- About one in 50 human beings carry beta thalassaemia. World-wide there are over a hundred million carriers. About one in 50 human beings carry beta thalassaemia: world-wide there are over a hundred million carriers.
- World-wide about 100,000 children are born each year with beta thalassaemia major or intermedia.
- In the UK there are about 200,000 carriers of beta thalassaemia and 764 people with beta thalassaemia major or intermedia. (Figures are for the beginning of the year 2000.)
- Carriers are particularly common among people who originate from the Mediterranean area, the Middle East or Asia. They are uncommon among people who originate from Northern Europe.

The table shows the carrier frequency in selected population groups.

Population group and area of origin	**Frequency of beta thalassaemia carriers**	**% of beta thalassaemia carriers**
Northern Europe	1 in 1,000	0.1
Mediterranean area:		
Cyprus	1 in 7	17
Italy (varies by region)	1 in 8 to 1 in 100	1-12
Greece	1 in 12	8
Portugal	1 in 50 to 1 in 100	1-2
Middle East:		
Egypt, Lebanon, Gulf States	1 in 30	3
Iran: varies by region	1 in 8 to 1 in 50	2-12
Indian sub-continent:		
India: varies by group	1 in 10 to 1 in 50	2-10
Pakistan: varies by region	1 in 8 to 1 in 50	2-10
Bangladesh	1 in 33	3
Sri Lanka	1 in 33	3
South East Asia:		
Southern China, Taiwan, Thailand, Cambodia, Laos	1 in 33	3
Malaysia, Indonesia: varies by region	1 in 33 - 1 in 100	1-3
West Africa: varies by region	1 50 to 1 in 100	1-2
Caribbean Area: varies by island	1 in 50 to 1 in 200	0.5-2

Carrying beta thalassaemia

(also known as having beta thalassaemia trait, or beta thalassaemia minor)…

… is not an illness, and will never become an illness. It was passed to you by one of your parents and you could pass it on to your children.

There is nothing to worry about, unless your partner is also a carrier.

- If your partner is also a carrier, together you could have children with a serious inherited illness. However, with medical help, a couple who are both carriers can have healthy children.
- If you are thinking of having children, your partner should have a blood test “for haemoglobin disorders”.
- If you have children or brothers and sisters, they could carry beta thalassaemia like you. Encourage them to have the same blood test.

To find out more, see your GP or a specialist counsellor.