Thalassaemia and Hb E Guide

What this leaflet is about: what thalassaemia and haemoglobin E are, how they are inherited, what the main forms are, and how they are treated.

Quick emergency advice

If a child looks pale, listless, is growing slowly, has a yellow tinge to the skin or the whites of the eyes, or has a swollen abdomen, please have them tested. Thalassaemia and haemoglobin E are inherited conditions, and finding the carrier state early prevents a surprise later.
Thalassaemia major and Hb E/beta-thalassaemia need lifelong care. Please keep every appointment, and contact the clinic if your child is unwell - fever, breathlessness, or a sudden increase in abdominal swelling.

What is thalassaemia?

Thalassaemia is an inherited disorder of haemoglobin, the red protein in your red cells that carries oxygen round the body. Haemoglobin is made of protein chains, and there are two types - the alpha chains and the beta chains. In thalassaemia, the genes that make one of these chains are missing or switched off, so too few of that chain are produced. The remaining chains cannot pair up properly, and the red cells that are made are fragile. They break down early in the spleen, so the number of red cells in the blood falls and the person becomes anaemic. The cells that are made are also unusually small, which is a useful clue on a blood film.

Why testing matters

Thalassaemia is the most common genetic disease in the world. In Asia, up to 1 in 7 people are carriers. Most carriers have never been tested and do not know that they carry the gene, because they usually feel completely well. When two carriers have a child together, that child may have thalassaemia major, which is a serious lifelong illness. That is why carrier testing is offered, and why it is recommended before starting a family or during pregnancy.
A carrier usually has only mild anaemia, and their red cells are smaller than usual. The blood film shows microcytosis, and the raised red cell count and reduced haemoglobin are easy to mistake for iron deficiency, which is the most common problem with recognising thalassaemia carriers. A specific test - a haemoglobin electrophoresis or high performance liquid chromatography, and sometimes genetic testing - makes the diagnosis.

How common is it in Malaysia?

Condition	Carrier rate in Malaysia
Alpha-thalassaemia	1.8 to 7.5 percent
Beta-thalassaemia	3 to 5 percent
Haemoglobin E (Hb E)	5 to 46 percent

Source: Malaysian Thalassaemia Registry 2009. The figures for Hb E vary widely between communities and regions, which is why the range is so broad.

Inheritance

Thalassaemia is inherited in a straightforward way: a child receives one set of genes from each parent. The pattern of inheritance is what makes it possible to predict what a couple's children are likely to have.

If one parent is a carrier and the other is not

For each pregnancy: 0 percent affected, 50 percent carrier, 50 percent unaffected non-carrier. In practice, about half the children will be carriers, and none will have the disease.

If both parents are carriers of the same type

For each pregnancy: 25 percent affected, 50 percent carrier, 25 percent unaffected non-carrier. This is the situation that can produce thalassaemia major, and it is why genetic counselling and partner testing matter so much.

Beta-thalassaemia: the main forms

Form	What it means
Trait or minor (carrier state)	One normal beta-globin gene and one abnormal one. Mild anaemia with small red cells. Usually no treatment at all is needed, and it is often only found out by chance on a blood test. Not transfusion dependent.
Major	Two abnormal beta-globin genes. The marrow cannot make enough haemoglobin to keep the person well after infancy, so lifelong blood transfusion is needed. Transfusion dependent.
Intermedia	Two abnormal genes, but enough haemoglobin is still made in between transfusions to keep the person reasonably well. Not transfusion dependent, though some people need transfusions occasionally. The condition is usually milder than major.
Compound heterozygotes	Two different abnormal genes inherited from each parent, for example Hb E/beta-thalassaemia or Hb S/beta-thalassaemia. The severity is variable, from mild to severe, and it cannot be predicted from the genes alone. Hb E/beta-thalassaemia is very common in Malaysia.

Alpha-thalassaemia: the main forms

Form	How many genes are missing	What it means
Silent carrier	1 gene deletion	No anaemia, no symptoms, and usually no treatment. It is found only on genetic testing, because a routine blood test looks normal. Not required.
Trait	2 gene deletions	Mild anaemia with small red cells, usually with no symptoms at all. Not required. This is the commonest form found in routine screening.
Hb H disease	3 gene deletions	Moderate anaemia that varies from person to person. Treatment is supportive: folic acid, and blood transfusion occasionally in some people. Occasionally required.
Hb H and Constant Spring	3 gene deletions plus Constant Spring	Variable severity, usually in between Hb H disease and the severe form. Occasionally required, with transfusion in some people.
Hydrops fetalis	4 gene deletions	The most severe form, called Hb Bart's hydrops fetalis. The fetus cannot make any haemoglobin and cannot survive. It is fatal in utero or at birth, and the management involves counselling and, where appropriate, care around the time of birth.

Thalassaemia major: treatment

- Lifelong blood transfusion, usually about every 3 to 4 weeks, to keep the haemoglobin and the blood count at a safe level. This is called maintaining a transfusion-dependent state, and the transfusions are given as day-case treatment.
- Iron chelation, to remove the iron that builds up from repeated transfusions. Without it, iron overload damages the heart, the liver and the endocrine glands, and it is the main cause of death in well-treated thalassaemia. Chelation is discussed in more detail below.
- A stem cell transplant, which can be a genuine cure, where a suitable matched donor exists. This is a once-only treatment and is usually considered for children with a matched sibling.
- Splenectomy, which is sometimes needed if the spleen is removing the transfused red cells too quickly, or if transfusion requirements rise. It reduces transfusion needs but increases the risk of certain infections, so it is used carefully and with vaccination.
- Folic acid, and regular monitoring of the heart, liver, thyroid, bone density, growth, hearing, vision and teeth.

Iron chelation

Each unit of transfused red cells contains about 200 to 250 mg of iron. The body has no natural way of getting rid of excess iron, so iron chelators are essential. Modern chelation is well tolerated, and a chelator can be chosen to suit the individual.

Medicine	Brand name	Usual strength and how it is given
Deferoxamine	Desferal	500 mg, given by infusion through a small portable pump over several hours, several nights a week. It is given into the skin of the abdomen or thigh, or into a vein. It is the most widely used and most familiar medicine, and it is very effective.
Deferasirox	Exjade	125 mg, 250 mg or 500 mg, given once a day as a dispersible tablet dissolved in water or juice, or as a film-coated tablet. It is taken by mouth, which is much more convenient than a pump.
Deferiprone	Ferriprox	500 mg, given as a tablet by mouth, usually in divided doses through the day. It is taken orally and is an effective alternative option.

Signs to watch for in a child

Thalassaemia major usually becomes apparent in the first year of life, as the haemoglobin made before birth and the small amount of fetal haemoglobin used in early infancy runs out. Ask your doctor about any of the following, and ask for a haemoglobin electrophoresis test if you are not sure.

- Pallor - unusual paleness of the skin, the palms and the inside of the lower eyelids, and of the gums.
- Listlessness, tiredness, poor feeding, and a baby who tires during feeding or sleeps much of the time.
- Jaundice - a yellow tinge to the skin and to the whites of the eyes.
- Slow growth, poor weight gain, and delayed milestones.
- An enlarging abdomen, caused by an enlarged liver and spleen as the body tries to cope with a low red cell count.
- Frequent infections, which become more common as the spleen enlarges.
- Dark urine, and a very brisk bowel habit, both from the breakdown of red cells.

The main causes of death if thalassaemia is not treated
Heart failure, caused by severe anaemia and by iron overload.
Severe infection.

In a well-treated patient with regular transfusions, good chelation and careful follow-up, most people now live into adulthood, many work, many raise families, and the outlook continues to improve. It depends on keeping the appointments, and that is the part of the treatment that is most in your hands.

Haemoglobin E

Haemoglobin E, or Hb E, is a variant of haemoglobin that is extremely common in South-East Asia, and in Malaysia in particular. On its own it is usually harmless. A person with Hb E trait has one Hb E gene and one normal gene, usually has no anaemia at all, and needs no treatment. It is a routine finding on a haemoglobin electrophoresis. The important point about Hb E is that it combines with other abnormal genes. Hb E/beta-thalassaemia, when one parent passes on an Hb E gene and the other passes on a beta-thalassaemia gene, is a significant condition that can range from mild to severe, and it is common in Malaysia. Hb E/beta-thalassaemia, and Hb E with a compound state such as Hb Constant Spring, are among the commonest severe inherited anaemias in the country.

> **Genetic counselling is advised**
> If Hb E trait is found on your blood test, and especially if your partner carries any form of thalassaemia or Hb E, please ask for genetic counselling before you plan a family. The counselling takes time, and the information about your own and your partner's genes allows the risk to your children to be calculated accurately and the options explained.

When to contact us

If you are worried about yourself, or about the person you are caring for, please get in touch. We would always much rather hear from you early than late. If you have read something in this leaflet that worries you, that is a good reason to telephone us, even if you feel well.

Visit us
Dr K Y Goh Haematology & Internal Medicine Clinic
Consultant Haematologist & Stem Cell Transplant Physician
KPJ Ampang Puteri Specialist Hospital
No. 1 Jalan Memanda 9, Taman Dato' Ahmad Razali,
68000 Ampang, Selangor, Malaysia

Telephone and fax
Tel: +60 3 4289 5000
Tel: +60 3 4270 2500
Fax: +603 4270 2938

Email
apsh@kpjampang.com
haemapsh@gmail.com

If you cannot reach us, or you are very unwell

Please go to the emergency department of KPJ Ampang Puteri Specialist Hospital, or call the emergency ambulance service. Do not wait for a routine appointment, and do not wait for a reply to an email.

Important medical disclaimer

This leaflet is written for patients and their families and carers. It is general patient education only. It is not a substitute for medical advice, and it is not a substitute for the diagnosis and treatment that your own haematologist, nurse, pharmacist or doctor will give you.

Nothing in this leaflet should be used to change, stop or start a medicine, a test or a treatment. If anything you read here is different from what your healthcare team has told you, follow your healthcare team and ask us about the difference.

Information about medicines names, strengths, test turnaround times and supportive care is current at the time this leaflet was prepared. It may be updated from time to time, and the version printed here may therefore not be the newest one. Please ask reception for the current copy.

If you think that you or someone you care for is seriously unwell, do not wait for an appointment and do not wait for this leaflet to be read. Contact the clinic, or go to the emergency department of KPJ Ampang Puteri Specialist Hospital, straight away.

We Listen. We Care. Evidence-based Medicine.

Dr K Y Goh Haematology & Internal Medicine Clinic | KPJ Ampang Puteri Specialist Hospital | Tel: +60 3 4289 5000

This leaflet is patient education only - it is not a substitute for medical advice.