Beta-thalassaemia

Key facts

- Thalassaemias are a group of genetically inherited conditions of haemoglobin, characterised by a reduced synthesis (production) of a globin chain. The most common of these is a reduction in the alpha (alpha thalassaemia) or beta (beta-thalassaemia) globin chain of the haemoglobin molecule.
- Beta-thalassaemia is an autosomal recessive condition and is caused by a variant of the beta globin gene.
- Beta-thalassaemia major is the most severe of the beta-thalassaemia disease states, and is the most common of the thalassaemias seen in the UK. It is suspected in an infant or child if, in the first two years of life, the child presents with severe microcytic anaemia, hepatosplenomegaly, difficulty feeding, lethargy, persistent diarrhoea and a failure to thrive.
- Treatment requires regular blood transfusions; these help to maintain normal growth and development. Without treatment, affected children fail to thrive, and will not survive beyond the age of 5-10 years.
- The condition is extremely variable, and symptoms in an affected individual often correlate to specific genetic alterations.
- Beta-thalassaemia is common in people from the Mediterranean, the Middle East, Southeast Asia and the Indian sub-continent; it is also seen, though less commonly, in those from sub-Saharan Africa.
- Testing for beta-thalassaemia is available across the UK and can be provided by the GP, at a local sickle cell and thalassaemia centre or via referral to a regional genetics centre.
- Antenatal screening for thalassaemia is available throughout the UK (except in Northern Ireland), and is part of the national antenatal screening programme.

Clinical features

- Individuals with beta-thalassaemia major are healthy at birth, but develop a severe anaemia between three months and one year of age; fetal haemoglobin (HbF) levels start to diminish, and adult haemoglobin (HbA) is synthesised in an increasing quantity.
- If undiagnosed, these babies often present with lethargy, feeding difficulties, pallor, diarrhoea and a failure to thrive.
- With correct treatment, children born in the UK with beta-thalassaemia major should expect to live to a near-normal life expectancy.
- Clinical manifestations are extremely variable.

Diagnosis

- The diagnosis depends on measuring red blood cell indices to reveal microcytic hypochromic red blood cells. Subsequent investigations should include a peripheral blood film that shows an excess of primitive nucleated red blood cells, and haemoglobin electrophoresis that demonstrates decreased amounts of adult haemoglobin (HbA) and persisting high amounts of fetal haemoglobin (HbF) after 12 months of age.
- DNA testing (see below) may be useful for predicting the clinical phenotype in some cases.

Genetic basis

- Beta-thalassaemia is an autosomal recessive condition, which means that an affected individual has two altered copies of the beta globin gene. Usually the individual's parents have one altered copy and one normal copy of the beta globin gene; these individuals are carriers of beta-thalassaemia (this is sometimes referred to as a beta-thalassaemia 'trait').
- The red cells of carriers are hypochromic and microcytic, resulting in a mild anaemia, but carriers generally do not require medical treatment.
- Each time a couple who are both carriers of beta-thalassaemia are expecting a child, there is a 25% (one-in-four) chance that the child could inherit the altered gene from each parent and be at risk of developing complications associated with the condition.
- To date, more than 200 thalassaemia disease-causing alterations have been identified in the beta globin gene. However, between 4 and 10 of these account for the majority of cases in the population groups where beta-thalassaemia is most common.
- Beta-thalassaemia can be co-inherited with other mutations that affect the beta globin gene, for example, if one parent is a carrier of the beta globin gene and the other parent is a carrier of the sickle globin gene, there is a 25% (one-in-four) chance that their child can inherit sickle beta-thalassaemia disease, which is a form of sickle cell disease. The severity of this combination is dependent on the type of beta-thalassaemia variant that the person has inherited.
- Being a carrier of beta-thalassaemia is thought to provide some protection against malaria.
- Testing for beta-thalassaemia is available across the UK and can be provided by the GP, at a local sickle cell and thalassaemia centre or at a regional genetic centre.
- Antenatal screening for thalassaemia is available throughout the UK (except in Northern Ireland) as part of the national antenatal screening programme.

Genetic testing

Genetic testing can be used to:

- identify the specific beta-thalassaemia gene variant following a molecular laboratory diagnosis of beta-thalassaemia;
- provide information about the genetic status of the relatives of someone identified with beta-thalassaemia following testing; and
- offer prenatal and pre-implantation genetic diagnosis:
    - » Prenatal diagnosis is usually possible by chorionic villus sampling (CVS) or amniocentesis. If a couple are considering prenatal diagnosis, referral should be made to the local clinical genetics or specialist haemoglobinopathy service prior to conception of a pregnancy, or as early as possible in a pregnancy. This ensures that appropriate advice and investigations are undertaken, and confirms whether an individual or couple are at risk of having an affected fetus, and whether prenatal diagnosis is possible.
    - » All couples considering pre-implantation genetic diagnosis must be referred to their local clinical genetics or haemoglobinopathy service.
- Genetic testing is available across the UK and referral can be arranged by the GP, specialist haemoglobinopathy centres, or via regional genetic centres.

Clinical management

- Those with beta-thalassaemia major require regular blood transfusion approximately every four-to-six weeks, usually starting between six months and two years of age, and continuing throughout childhood and adulthood.
- The transfused blood provides vital red blood cells to help suppress the bone marrow production of immature and ineffective thalassaemic red blood cells, which are ineffective in transporting vital oxygen to body tissues and organs and can cause complications.
- Due to continued absorption of iron in the diet (compounded by additional iron derived from the transfused blood), these individuals become grossly iron overloaded which can cause complications affecting all major organs of the body and fatality in the long term.
- To manage iron overload, adjunct therapy is required using oral medications such as deferasirox, subcutaneous iron chelator desferioxamine and other treatments.
- Regular outpatient management from birth, and throughout adulthood, is crucial to ensure adequate monitoring and management of those with beta-thalassaemia.

Direction to further reading, guidelines and patient groups

- For detailed and comprehensive guidance in the management of thalassaemia, a document from the United Kingdom Thalassaemia Society is available to view and download.
- Information on the UK Screening Programme can be found here.
- For sources of further support and information, contact the national voluntary organisation:

  United Kingdom Thalassaemia Society
  19 The Broadway
  Southgate
  London N14 6PH
  Tel: 020 8882 0011
  Website: ukts.org

This information is intended for educational use and was current in March 2020. For clinical management, it is recommended that local guidelines and protocols are used.

Produced in collaboration with Birmingham Women's NHS Foundation Trust's Clinical Genetics department and Brent Sickle Cell & Thalassaemia Centre, London North West University Healthcare NHS Trust.