THALASSAEMIA FROM 'A' TO 'Z'

A comprehensive e-glossary for patients with thalassaemia
**α-thalassaemia:** An inherited disorder characterized by reduced or suppressed production of α-globin chains. The haemoglobin molecule is composed of (4) α-globin chains and (2) β-globin chains. When the genetic defect affects one or more of the α-globin chains, the patient has α-thalassaemia, which increases in importance according to the number of α-globin chains that are not produced. Clinical significance occurs when 3 or 4 chains are missing.

**Abdominal ultrasound:** A non-invasive procedure that examines internal organs.

**Adenine:** One of the four bases that make up DNA, abbreviated with an 'A'.

**Adherence (patient):** Adherence to (or compliance with) a medication regimen is generally defined as the extent to which patients take medications, as prescribed/advised by their physician. It denotes choice and mutuality in goal setting, treatment planning, and implementation of the regimen.

**Adult haemoglobin (HbA):** It is the most common human haemoglobin tetramer. It contains two α-subunits and two β-subunits, accounting for over 97% of the total red blood cell haemoglobin.

**Agranulocytosis:** Also known as “agranulosis” or “granulopenia”, it is an acute condition involving a severe and dangerous lack of a certain type of infection-fighting white blood cells (granulocytes). People with this condition are at very high risk of serious infections, due to their suppressed immune system.

**Alloimmunization:** A common complication of transfusion therapy, occurring in as many as 10-20% of patients with thalassaemia. Alloimmunisation is more common in children who begin transfusion therapy after 1-3 years of age than in those who begin
transfusion therapy earlier. Some evidence also suggests that new alloantibodies develop more frequently after splenectomy (Thompson 2011). The use of extended antigen matched donor blood is effective in reducing the rate of alloimmunization.

**Alpha globin:** A blood protein found in the red blood cells. A and β-globins combine to make haemoglobin, which carries oxygen.

**Anaemia:** A medical condition causing a decrease in the total amount of red blood cells (RBCs) or haemoglobin in the blood with a lowered ability of the blood to carry oxygen.

**Arrhythmia:** An irregular heart rhythm. Iron overload can cause cardiac problems and is actually the most common cause of cardiac problems in thalassaemia. If excess iron is deposited in the heart, it can interfere with the heart’s ability to conduct electrical signals, causing arrhythmia.

**β-globin:** A blood protein found in red blood cells that when absent or at abnormally low levels leads to the condition known as thalassaemia. B and α-globins combine to make haemoglobin, which carries oxygen.

**β-thalassaemia:** It is the most serious form of the inherited thalassaemias, where no or very little β-globin is produced. B-thalassaemia includes 3 main forms; thalassaemia major or transfusion dependent thalassaemia (TDT), variably referred to as “Cooley’s anaemia” or “Mediterranean anaemia”, thalassaemia intermedia or non-transfusion dependent thalassaemia (NTDT) and thalassaemia minor, also called “β-thalassaemia carrier”, “β-thalassaemia trait” or “heterozygous β-thalassaemia”. This categorization depends on the range of the disease’s severity.
**Bases:** Small molecules inside a larger molecule of DNA. Bases – Adenine (A), Cytosine (C), Guanine (G), and Thymine (T) – are combined in pairs in a DNA molecule (e.g. CGGTACAGG) and encode instructions for making proteins.

**Biopsy:** An examination of tissue removed from a living body to discover the presence, cause, or extent of a disease.

**Biosimilar (medicine/drug):** A drug manufactured on the basis of already licensed biological drugs and using the information from clinical trials that biological products have previously undergone.


**Bisphosphonates:** A group of drugs that prevent the loss of bone density. They are the most commonly prescribed drugs used to treat osteoporosis and similar diseases.

**Blood:** A vital fluid that brings nourishment to the body’s organs and tissues and carries away waste substances. Blood transports oxygen, helps the body fight infection, transports hormones, delivers nutrients and disposes of waste.

**Blood Bank:** A center where blood, gathered as a result of blood donation, is stored and preserved for later use in blood transfusion. The term "blood bank" typically refers to a division of a hospital where the storage of blood product occurs and where proper testing is performed (to reduce the risk of transfusion related adverse events).

**Blood Transfusion:** The process of transferring blood or blood products into one’s circulation intravenously. Transfusions are used for various medical conditions to replace lost components of the blood. Regular blood transfusions greatly contribute to the quality and length of life of patients with thalassaemia major, and have been a central aspect of the treatment of thalassaemia since the 1960s.

**Bone Marrow:** The soft, gelatinous tissue that fills the cavities of bones. Bone marrow is either red or yellow, depending upon the preponderance of hematopoietic (red) or fatty
(yellow) tissue. It is the primary site of new blood cell production (haematopoiesis), producing approximately 500 billion blood cells per day. In adult humans, bone marrow is primarily located in the ribs, vertebrae, sternum, and bones of the pelvis.

**Bone Marrow expansion:** One of the most important effects thalassaemia, which causes bones widening. This can result in abnormal bone structure, especially in the patient’s face and skull. Bone marrow expansion also makes bones thin and brittle, increasing the chance of bone fracture. Occasionally, and if blood transfusion is inadequate, the expansion can occur outside the marrow cavity (extramedullary).

**Bradycardia:** A condition where the heart rate is slower than normal. The hearts of adults at rest usually has a rate between 60 and 100 beats per minute (BPM).

**Cardiologist:** A specialist in the branch of medicine that deals with the disorders of the heart as well as some parts of the circulatory system. The field includes medical diagnosis and treatment of congenital heart defects, coronary artery disease, heart failure, valvular heart disease and electrophysiology, which deals with arrhythmias.

**Cardiomyopathy:** A term referring to the diseases of the heart muscle, causing it to become enlarged, thick or stiff, but also weak and unable to pump blood effectively to all parts of the body.

**Caregiver:** An unpaid or paid member of a person’s social network who helps them with activities of daily living. Caregiving is most commonly used to address impairments related to old age, disability, a chronic illness or disease, or a mental disorder.
**Carrier:** An individual who harbors the causative agent of an infectious or genetic disease, without manifesting any symptoms, but is capable of transmitting the infection or the genetic defect; the condition of such an individual is referred to as “the carrier state”.

**Chelating agent:** A chemical compound that binds tightly to metal ions. In medicine, chelating agents are used to remove toxic metals from the body.

**Chromosome:** A rod-shaped or threadlike DNA-containing structure, found in the nucleus of cells. Chromosomes carry inherited information in the form of genes, which govern all cell activity and function. Humans have 46 chromosomes. In the case of β-thalassaemia, the affected gene is located on chromosome 11.

**Chronic:** A term used in medicine to refer to any disease or condition that persists over time or is frequently recurring.

**Cirrhosis:** A late stage of scarring (fibrosis) of the liver caused by many forms of liver diseases and conditions, such as hepatitis, chronic alcoholism or iron overload.

**Clinical studies/trials:** Clinical studies are research studies that test or observe how well medical approaches work in patients. Some clinical studies test new treatments, such as a recently developed drug or medical therapy. Moreover, these studies help researchers learn if a new treatment is effective or less harmful than standard treatments, and identify potentially unwanted side effects.

See also: [https://www.centerwatch.com/images/infographics/Understanding-Clinical-Trials-Infographic-low.png](https://www.centerwatch.com/images/infographics/Understanding-Clinical-Trials-Infographic-low.png)

**Cooley’s anaemia:** Another name for the condition known as β-thalassaemia or thalassaemia major. It derives from the name of Dr. Thomas Benton Cooley, an American physician specializing in paediatrics and haematology and one of the first doctors who described the condition.
**Communicable (disease):** A disease spread from one person to another through a variety of ways that include contact with blood and bodily fluids, breathing in an airborne virus or bacterium or by being bitten by an insect.

**Counterfeit (medicine/drug):** A medication or pharmaceutical product which is deliberately and fraudulently mislabeled with respect to its stated use. Counterfeit drugs have rarely been efficacious but are often dangerous and detrimental to public health.  

**Cytosine:** One of the four bases that make up DNA, abbreviated with a 'C'.

**DEXA Scan:** The dual-energy X-ray absorptiometry (DEXA Scan) is a high-precision type of X-ray that uses a very small dose of ionizing radiation to produce pictures of the inside of the body (usually the lower spine and hips), in order to measure bone mineral density and bone loss. It is used to diagnose or assess the risk of osteoporosis.

**DNA:** Abbreviation for deoxyribonucleic acid, DNA is the organic chemical of complex molecular structure that is found in all cells and in many viruses. DNA codes genetic information for the transmission of inherited traits.

**Deferasirox:** Deferasirox is an oral iron chelator. Its main use is to reduce chronic iron overload in patients who are receiving long-term blood transfusions for conditions, such as β-thalassaemia and other chronic anaemias.
**Deferiprone:** Deferiprone is an oral iron chelator used as an agent in thalassaemia syndromes, when iron overload from blood transfusions occurs.

**Deferoxamine:** Deferoxamine or desferrioxamine (brand name: Desferal) is an iron chelating agent used to treat transfusion related chronic iron overload. It is specifically used in iron overdose, hemochromatosis, overload due to multiple blood transfusions or an underlying genetic condition, and aluminium toxicity in people on dialysis.

It was the first chelation drug to get approval both in the U.S. and Europe and for many years was the only chelating option for patients. Unlike Deferasirox and Deferiprone, Defereroxamine is not available for oral use and it is administered subcutaneously, thus by slow infusion under the skin.

**Delayed puberty:** It is one of the most obvious clinical consequences of iron overload. Delayed puberty is defined as the complete lack of pubertal development in girls by the age of 13, and in boys by the age of 14.

**Delta globin:** A blood protein found in the red blood cells. And a component of the Hb molecule. Alpha and γ-globins combine to make haemoglobin A2 - a secondary adult haemoglobin used to carry oxygen, normally less than 3% of the Hb molecule.

**Dental caries:** A demineralization of the tooth surface caused by bacteria. Symptoms may include pain and difficulty with eating, while complications may include inflammation of the tissue around the tooth, tooth loss, and infection or abscess formation. The caries prevalence has been found to be significantly higher in thalassaemic patients than in healthy individuals (Hattab 2001). The higher dental caries experienced in β-thalassaemia major patients may be attributed to poor oral hygiene, improper dietary habits, lack of dental awareness, reduced salivary flow rate, and neglected dental care.

**Diabetes:** A group of metabolic disorders characterized by a high blood sugar level over a prolonged period. Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced. Chronic diabetes conditions include type 1 diabetes and type 2 diabetes. According to the World Health Organization (WHO), in 2016 diabetes was the direct cause of 1.6 million deaths worldwide. It can be a complication of thalassaemia, especially with increasing age.
**Disease registry:** A special database that contains information about people diagnosed with a specific type of disease. Most disease registries are either hospital-based or population-based. A hospital-based registry contains data on all the patients with a specific type of disease diagnosed and treated at that hospital. A population-based registry contains records for people diagnosed with a specific type of disease who reside within a defined geographic region.

**Dominant:** A term referring to genetic disorders in which a person only needs one copy of the mutated gene to develop the disorder. This means that only one parent is needed to transmit the condition to a child, who will be clinically affected.

**Echocardiography:** A test that uses sound waves to produce live images of the heart. The produced image is an echocardiogram. This test allows doctors to monitor how the heart and its valves are functioning.

**Electrocardiogram (ECG):** A diagnostic tool that is routinely used to assess the electrical and muscular functions of the heart. While it is a relatively simple test to perform, the interpretation of the ECG tracing requires a significant amount of training.

**Electronic Health Record (EHR):** The systematized collection of patient and population electronically-stored health information in a digital format. These records can be shared across different health care settings. EHRs may include a range of data, including demographics, medical history, medication and allergies, immunization status, laboratory test results, radiology images, vital signs, personal statistics like age and weight, and billing information.
**Endemic:** In epidemiology, an infection or a disease is said to be endemic in a population when that infection/disease is constantly maintained at a baseline level in a geographic area without external input. Thalassaemia is endemic among Mediterranean and Asian populations, whilst sickle cell disease (SCD) is endemic in individuals of African origin.

**Endocrinology:** The branch of biology and medicine dealing with the endocrine system, its diseases, and its specific secretions known as hormones. It is also concerned with the integration of developmental events such as growth, lactation, and reproduction, which are regulated by hormones.

**Epidemiology:** The branch of medicine which deals with the incidence, distribution, and possible control of diseases and other factors relating to health.

**Erythropoietin (EPO):** Also known as “haemopoietin”, erythropoietin is a glycoprotein cytokine secreted by the kidney in response to cellular hypoxia; it stimulates red blood cell production (erythropoiesis) in the bone marrow. Common causes of cellular hypoxia resulting in elevated levels of EPO (up to 10,000 mU/mL) include any anaemia and hypoxemia, due to chronic lung disease.

**Extramedullary haematopoiesis (EMH):** It is the formation and development of blood cells outside the medullary spaces of the bone marrow.

**Ferritin:** A protein in the body that binds to iron, produced by the liver. A simple blood test to monitor the patient’s ferritin level is a convenient way to check on the amount of iron in the blood. This test is used to provide a general picture of how effective chelation is on a day-to-day basis, in thalassaemia and other iron loading conditions.
In general, most haematologists set a goal of a ferritin level of 1,000 or below for their thalassaemia patients. Nowadays, thanks to scientific advances and greater chelating options, the possibility of reaching lower ferritin levels has significantly increased.

**Fetal or foetal haemoglobin (HbF):** It is the main oxygen transport protein in the human fetus during the last seven months of development in the uterus and persists in the newborn until roughly 2-4 months old. Functionally, fetal haemoglobin differs most from adult haemoglobin in that it is able to bind oxygen with greater affinity than the adult form, giving the developing fetus better access to oxygen from the mother’s bloodstream.

Fetal haemoglobin is nearly completely replaced by adult haemoglobin by approximately 6 months postnatally, except in thalassaemia cases in which there may be a delay in cessation of HbF production.

**Fibrosis:** A condition marked by an increase in fibrous tissue, also known as ‘scar tissue’. Iron overload, due to frequent blood transfusions and/or inadequate chelation, could result in the formation of an abnormally large amount of scar tissue in the liver and lead to fibrosis. Severe scarring of the liver could cause cirrhosis, a serious condition that can result in liver failure.

**Folic Acid:** A form of a water-soluble vitamin B. Folic acid is used for preventing and treating low blood levels of folate (folate deficiency), as well as its complications, including anaemia and the inability of the bowel to absorb nutrients properly. It is a component in the formation of the DNA molecule. For this reason, it becomes deficient in conditions where massive cell destruction takes place, such as untreated thalassaemias.

**Gamma globin:** A blood protein found in the red blood cells. Alpha and γ-globins combine to make haemoglobin F -- the type of haemoglobin most dominant in fetal life for carrying oxygen.
See also: Haemoglobin F (HbF)

**Generic (drug):** A medication created to be the same as an existing approved brand-name drug in dosage form, safety, strength, route of administration, quality, and performance characteristics.

**Genes:** The biological units of inheritance, the unique blueprints for an individual organism, providing all the biological information needed for controlling growth and development throughout its life. Genes contain DNA and they are in each person’s cells. They specify the person’s characteristics such as the colour of their eyes, characteristics of their face and many more. Each gene is a code for a specific protein.

**Gene Therapy:** An approach that aims to cure genetic diseases, by replacing or correcting (editing) a defective or non-functional gene in the patient’s DNA. In the case of β-thalassaemia, a defect (mutation) in the β-globin gene results in the decrease or absence of haemoglobin, the vital oxygen-carrying protein of the body. If this gene is replaced by a functional one, then it is anticipated that haemoglobin production will be restored and, consequently, the patient’s red blood cells (RCBs) will have a normal function.


**Genotype:** The genetic composition of a person. Usually used when considering one gene or chromosome (e.g., males have a XY genotype, females have a XX).

**Guanine:** One of the four bases that make up DNA, abbreviated with a ‘G’.

**Guideline (medical):** Also called a “clinical guideline” or “clinical practice line”, a medical guideline is a document with the aim of guiding decisions and criteria regarding diagnosis, management, and treatment in specific areas of healthcare. In contrast to previous approaches, which were often based on tradition or authority, modern medical guidelines are based on an examination of current evidence within the paradigm of evidence-based medicine.
**Haem:** A deep red iron-containing substance that binds to oxygen. There is one haem per beta or alpha globin and thus four haems per haemoglobin molecule.

**Haematologist:** A medical professional who has expertise in disorders that affect blood.

**Haemochromatosis:** The abnormal accumulation of iron in parenchymal organs, leading to organ toxicity and caused by the excessive accumulation of iron in tissues and organs impairing their function.

**Haemoglobin:** A protein found in red blood cells; two β-globins, two α-globins and four haemes combine to make one adult haemoglobin molecule. Haemoglobin carries oxygen from the lungs to the body’s tissues and returns carbon dioxide from the tissues to the lungs.

**Haemoglobin A (HbA):** Also known as “adult haemoglobin”, “haemoglobin A1” or “heamoglobin α2β2”, it is the most common human hemoglobin tetramer, accounting for over 97% of the total red blood cell haemoglobin.

**Haemoglobin A2 (HbA2):** A protein found in the red blood cell, two gamma globins, two alpha globins and four haems combine to make one haemoglobin A2 molecule. Haemoglobin A2 is the secondary adult haemoglobin used to carry and deliver oxygen to the cells. It constitutes only less than 3% of the total haemoglobin, but it rises to over 3,5% in thalassaemia carriers.

**Haemoglobin E (HbE):** An abnormal haemoglobin with a single point mutation in the β-chain. This is a variant haemoglobin which, in combination with a β-thalassaemia gene, will cause a thalassaemia syndrome of ranging severity.
**Haemoglobin F (HbF):** A protein found in the red blood cell, two delta, two alpha and four haems combine to make one haemoglobin F molecule. Haemoglobin F is the dominant fetal haemoglobin used to carry and deliver oxygen to the cells.

**Haemoglobin H (HbH) disease:** A moderate to severe form of α-thalassaemia characterized by pronounced microcytic hypochromic haemolytic anaemia. It is caused when 3 out of 4 α-globin genes are not functioning.

**Haemoglobin S (HbS):** It is the most common type of abnormal haemoglobin and the basis of sickle cell trait and sickle cell anaemia. Haemoglobin S in its heterozygous form (inherited from one parent only) confers some immunity to malaria to whom carries it, although it brings a deadly disease (sickle cell anaemia) in its homozygous form (inherited from both parents).

**Haemoglobinopathy:** A blood disorder caused by a genetically determined change in the molecular structure of haemoglobin. Thalassaemia and sickle cell disease belong to the broader haemoglobinopathies family.

**Haemopoietic Stem Cell Transplantation (HSCT):** More commonly known as bone marrow transplantation (BMT), it is the transplantation of multipotent hematopoietic stem cells, usually derived from bone marrow, peripheral blood, or umbilical cord blood. It may be autologous (the patient’s own stem cells are used), allogeneic (the stem cells come from a donor) or syngeneic (from an identical twin).

See also:  [https://thalassaemia.org.cy/publications/bone-marrow-transplantation-in-%ce%b2-thalassaemia-2018/](https://thalassaemia.org.cy/publications/bone-marrow-transplantation-in-%ce%b2-thalassaemia-2018/)

**Haemolysis:** The process of disintegration of red blood cells, which releases haemoglobin. Normally red blood cells disintegrate every 120 days. In conditions in which red blood cells disintegration occurs sooner, this results in haemolytic anaemia.
**Haemovigilance**: The set of surveillance procedures covering the entire blood transfusion chain, from the donation and processing of blood and its components, through to their provision and transfusion to patients, and including their follow-up.

**Heart Failure (HF)**: Also known as “congestive heart failure (CHF)” and ”congestive cardiac failure (CCF)”, is when the heart is unable to pump sufficiently to maintain blood flow to meet the body's needs. Heart failure can manifest itself in severe anaemias, such as in untreated thalassaemia or when the heart muscle id damaged due to iron overload.

**Hepatitis A**: An acute, usually benign liver inflammation caused by RNA-containing virus that does not persist in the blood serum and is transmitted by food and water contaminated with infected faeces. It can be prevented by vaccination.

**Hepatitis B**: A sometimes fatal liver inflammation caused by a double-stranded DNA virus that tends to persist in the blood serum and is transmitted by contact with infected blood or contact with other infected bodily fluids, (i.e. during sexual intercourse). It can be prevented by vaccination.

**Hepatitis C**: A viral infection that causes liver inflammation, caused by an RNA virus and usually transmitted by illicit drug use, blood transfusion or exposure to infected blood or blood products. In the majority of cases, hepatitis C leads to chronic infections and liver damage.

**Hepatologist**: A specialist in the branch of medicine called Hepatology, which includes the study of the liver, the biliary tree, the gallbladder and the pancreas. A hepatologist manages disorders in these areas. Hepatology was traditionally a subspecialty of gastroenterology, but recent advances in the understanding of this subspecialty have made it a field of its own.

**Hepcidin**: A small peptide hormone secreted by hepatocytes, circulating in blood plasma and excreted in urine. Hepcidin regulates iron concentration in the plasma and the distribution of iron among different tissues. Dysregulation of hepcidin production underlies many iron disorders. Hepcidin acts by regulating the cellular concentration of its receptor, ferroportin.
**Hereditary Disease:** A disease or disorder that is inherited genetically. Hereditary Diseases are passed on from one generation to another through defective genes. The chromosomes are responsible for passing the traits from the parent to the offspring.

**Hydrops Fetalis:** A severe, extensive, and life-threatening oedema (swelling), attributable to heart failure, that affects some fetuses and newborns, characterized by fluid accumulation in extravascular components and body cavities. There are two types of hydrops fetalis; immune and nonimmune. In α-thalassaemia, if all the 4 genes are inactive, Hb Bart’s hydrops fetalis can occur. In that case, the pregnant mother will suffer from high blood pressure and preeclampsia and could also be in danger. The fetus is usually stillborn, but can be saved by intra-uterine transfusion and be born to be transfusion-dependent.

**Hydroxyurea:** A myelosuppressive agent used in Sickle Cell Disease (SCD) to increase haemoglobin and reduce the frequency of acute painful episodes in patients. Hydroxyurea could also be beneficial for specific patient populations with non-transfusion-dependent thalassaemia (NTDT).

**Hypersplenism:** A condition in which the spleen becomes increasingly large and non-functional. This condition causes rapid and premature destruction of blood cells, included red cells, white cells and platelets.

**Hypogonadic hypogonadism (HH):** Hypogonadism, along with delayed puberty, are the most obvious clinical consequences of iron overload. It is defined in boys as the absence of testicular enlargement (less than 4 ml), and in girls as the absence of breast development by the age of 16. It is one of the most common endocrine complications in thalassaemia.

**Hypoparathyroidism (HPT):** It is the combination of symptoms caused by inadequate parathyroid hormone production. HPT has been considered as a typical complication of the second decade of life in transfusion dependent patients with thalassemia major. The incidence of HPT varies from centre to centre (from 1.2% to 19%) and HPT seems to affect men more frequently.
Hypothyroidism: Also called “underactive thyroid” or “low thyroid”, it is a disorder of the endocrine system in which the thyroid gland does not produce enough thyroid hormone. Hypothyroidism may not cause noticeable symptoms in the early stages. Over time, untreated hypothyroidism can cause a number of health problems, such as obesity, joint pain, infertility and heart disease. In patients with thalassaemia, this complication is mainly attributed to iron overload and is uncommon in optimally treated individuals.

Incidence: In epidemiology, incidence is a measure of the probability of occurrence of a given medical condition in a population within a specified period of time.

Ineffective erythropoiesis: It is active erythropoiesis with premature death of red blood cells, a decreased output of Red Blood Cells (RCBs) from the bone marrow, and, consequently, anaemia. Ineffective erythropoiesis is the hallmark of β-thalassaemia that triggers a cascade of compensatory mechanisms resulting in clinical sequelae such as anaemia, erythroid marrow expansion, extramedullary hematopoiesis, splenomegaly, and increased gastrointestinal iron absorption.

Infection: The invasion of an organism's body tissues by disease-causing agents, their multiplication, and the reaction of host tissues to the infectious agents and the toxins they produce. Infectious diseases, also known as “transmissible diseases” or “communicable diseases”, are illnesses resulting from an infection.

Innovative (medicine/drug): Also called “originator drugs” or “reference drugs”, they are medicinal products that have gone through three or more phases of rigorous clinical trials over almost two decades and are authorised by officially established regulatory agencies (EMA, FDA) to be marketed and used by healthcare professionals on humans.

See also: https://thalassaemia.org.cy/education/learn-about-drugs-and-drug-safety/
**Iron Chelation:** A therapy aiming to balance the rate of iron accumulation in a patient’s body from blood transfusion by the use of special drugs, called iron chelators. There are three iron chelators approved for use in most countries of the world; Deferoxamine (Desferal®), Deferasirox, and Deferiprone or L1 (Ferriprox™).

**Iron Overload:** A term that indicates accumulation of iron in the body. The most important causes causing iron overload are hereditary haemochromatosis (HHC), a genetic disorder, and transfusional iron overload, which can result from repeated blood transfusions. Iron accumulation is toxic to many tissues, causing heart failure, cirrhosis, liver cancer, growth retardation and multiple endocrine abnormalities.

**Labile plasma iron (LPI):** LPI represents a component of non-transferrin bound iron (NTBI) that is both redox active and chelatable, capable of permeating into organs and inducing tissue toxicity. LPI measurement can serve not only as an indicator of impending iron overload, but also as measures of the efficacy of iron chelation in eliminating a potentially toxic agent from plasma.

**Liver iron concentration (LIC):** Measurement of liver iron concentration (LIC) is the best parameter to assess iron deposits in the body. It is a key parameter to guide the clinical management of patients with primary or secondary haemochromatosis, characterized by iron overload. Several approaches have been used to quantify liver iron invasively (e.g. liver biopsy) and non-invasively (e.g. superconducting quantum interference devices (SQUIDs & MRI)).
Malaria: A mosquito-borne acute or chronic infectious disease caused by parasites in the red blood cells that affects humans and other animals.

Malignancy: A term for diseases in which abnormal cells divide without control and can invade nearby tissues. Malignant cells can also spread to other parts of the body through the blood and lymph systems. There are several main types of malignancy, most of which are used to characterize cancer.

Multidisciplinary care: A type of care which occurs when professionals from a range of disciplines work together to deliver comprehensive care that addresses as many of the patient’s health and other needs as possible.

Magnetic resonance imaging (MRI): A medical imaging technique used in radiology to form pictures of the anatomy and the physiological processes of the body.

Morbidity rate: The percentage of people who suffer from or have complications from a medical condition or after a procedure or treatment.

Mortality rate: A measure of the number of deaths (in general, or due to a specific cause) in a particular population, scaled to the size of that population, per unit of time.

Mutation: A change that occurs in the DNA sequence, either due to mistakes when the DNA is copied or as the result of environmental factors.
Neurologist: A medical specialist in the branch of medicine concerned with the study and treatment of disorders of the nervous system. Neurological complications in patients with thalassaemia have been attributed to various factors such as chronic hypoxia, bone marrow expansion, iron overload, and desferrioxamine neurotoxicity.

Neutropenia: It is a condition defined as the abnormally low concentration of neutrophils (a type of white blood cell) in the blood. People with neutropenia are more susceptible to bacterial infections and, without prompt medical attention, the condition may become life-threatening (neutropenic sepsis). In thalassaemia, it is mostly associated with Deferiprone treatment and hypersplenism.

Non-transferring bound iron (NTBI): NTBI is the term used for the free iron present in plasma, including all the forms of iron present in serum or plasma which are not bound to the serum transferrin (Tf) and the other traditional iron binding proteins like haem, apoferritin, hemosiderin etc. This unbound iron is the dangerous element causing toxicity to cells, especially in its labile form (see also LPI).

Osteoporosis: A condition characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequential increase in fracture risk. Osteoporosis is a prominent cause of morbidity in patients with thalassaemia major (TM), especially as they grow older. It is a major cause of pain.

Pathogen: An agent (such as virus, bacterium, or other microorganism) that can cause a disease.

Pathophysiology: A convergence of pathology with physiology, it is the study of the disordered physiological processes that cause, result from, or are otherwise associated with a disease or injury. Pathology is the medical discipline that describes conditions typically observed during a disease state, whereas physiology is the biological discipline that describes processes or mechanisms operating within an organism.

Pericarditis: An inflammation of the pericardium, which is the thin layer membrane-like tissue that surrounds the heart, holds it in place and helps it work.

Phenotype: An individual's observable characteristics, such as height, eye color, and blood type.

Pilot study: Also known as “pilot project”, “pilot test”, or “pilot experiment”, it is a small scale preliminary study conducted in order to evaluate feasibility, duration, cost, adverse events, and improve upon the study design prior to performance of a full-scale research project.

Plasma: The clear, straw-colored liquid portion of blood that remains after red blood cells, white blood cells, platelets and other cellular components are removed. It is the single largest component of human blood, comprising about 55%, and contains water, salts, enzymes, antibodies and other proteins.
Platelets: Small, colourless, disc-shaped cells released from the bone marrow into the blood. The principal function of platelets is to prevent bleeding. The blood usually contains about 140,000 to 440,000 platelets per microliter.

Prevalence: In epidemiology, prevalence is the proportion of a particular population found to be affected by a medical condition (typically a disease or a risk factor). It is derived by comparing the number of people found to have the condition with the total number of people studied, and is usually expressed as a fraction, as a percentage, or as the number of cases per 10,000 or 100,000 people.

Protein: A type of molecule produced by the body. The instructions for producing proteins reside in the genes.

Pulmonary hypertension: A condition occurring when the pressure in the blood vessels that carry blood from the heart to the lungs is higher than normal. It can affect people of all ages, but it is more common in people who already suffer from another heart or lung condition. It is encountered mainly in NTDT or sickle cell disease (SCD).

Radiologist: A medical specialist that uses medical imaging mainly to diagnose and also to treat diseases within the bodies of both humans and animals. A variety of imaging techniques such as X-ray radiography, ultrasound, computed tomography (CT), nuclear medicine including positron emission tomography (PET), and magnetic resonance imaging (MRI) are used to diagnose or treat diseases.

Recessive: A term referring to genetic disorders in which a person must have two copies of the mutated gene to develop the disorder. Thalassaemia is a recessive disorder, since both parents must be healthy carriers for an affected child to be born.
**Red Blood Cells (RBCs):** Also known as “erythrocytes” or “red cells”, they are cellular components of the blood. Their primary function is to carry oxygen from the lungs around the body, binding the oxygen to haemoglobin, which they then deliver it to each tissue and cell to keep them healthy and functioning. Approximately 84% of the cells in the human body are RBCs.

**Regulatory bodies/authorities:** A public organization or government agency that is set up to exercise a regulatory function. As far as medicinal products are concerned the US Food and Drug Organization (FDA) and the European Medicines Agency (EMA) are the world’s largest regulatory authorities. The FDA is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices. Accordingly, the EMA aims to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health in the European Union (EU).

**Sickle Cell Disease (SCD):** A group of genetic disorders that affect haemoglobin. People with these disorders have atypical haemoglobin molecules called haemoglobin S, which can distort red blood cells into a sickle, or crescent, shape, especially when oxygen is in short supply (hypoxia).

**Sickle Cell trait:** A condition in which a person has one abnormal form of the haemoglobin beta gene, but does not display the severe symptoms of sickle-cell disease that occur in a person who has two copies of that abnormal form of the haemoglobin beta gene. Such a person is a carrier and can have an affected child, if the partner is also an HbS or a β-thalassaemia carrier.
**Spleen:** An organ located in the upper left abdomen which forms part of the body’s lymphatic system. The spleen plays important roles in regard to all blood cells, acting as a filter when they are abnormal or about to disintegrate, and the immune system.

**Splenectomy:** The surgical procedure that partially or completely removes the spleen. Many patients with thalassaemia major require splenectomy. However, optimal clinical management from the time of diagnosis may delay or even prevent hypersplenism, thereby increasing the efficiency of transfusion therapy and reducing the need for splenectomy.

**Splenomegaly:** An abnormal enlargement of the spleen. Splenomegaly is one of the four cardinal signs of hypersplenism which include: some reduction in number of circulating blood cells affecting granulocytes, erythrocytes or platelets in any combination; a compensatory proliferative response in the bone marrow; and the potential for correction of these abnormalities by splenectomy.

**Substandard (medicine/drug):** A drug whose use has been authorized in a country, but its manufacturing has not followed the quality and safety protocols, and recommendations of official national, regional or international drug regulatory authorities. Therefore, the safety and effectiveness of substandard drugs are greatly questioned.


**Syphilis:** A chronic contagious disease, transmitted sexually, which produces chancre (painless ulcers), rashes and systemic lesions.

**T2 MRI or R2/FerriScan:** A non-invasive procedure that uses magnetic resonance imaging (MRI) to non-invasively measure iron in the liver. The T2 MRI, R2/FerriScan, and
liver biopsy methods all provide information on a patient’s liver iron concentration (LIC). In thalassaemia, maintaining an LIC of 7 or lower is desirable; LICs above 15 are indicative of serious iron overloading in the liver.

**Tachycardia:** A sort of arrhythmia characterized by relatively rapid heartbeat (usually faster than 100 beats per minute in adults).

**Thalassaemia:** A term referring to a group of genetically-inherited disorders of the blood, which cause a reduction of one or more of the proteins that make up the haemoglobin molecule. It is not infectious and cannot be passed from one individual to another by personal contact. It is a disorder of the haemoglobin molecules inside the red blood cells, which are inherited. The combination of one abnormal gene from the mother and one from the father leads to three different types of thalassaemia.

**Thalassaemia intermedia:** An inherited version of homozygous thalassaemia where some beta globin is made. The severity of the symptoms depends on how much beta globin is present, but most cases are not transfusion dependent until later in life.

**Thalassaemia major (TM):** The most serious of the inherited thalassaemias, occurring when a child inherits two mutated genes, one from each parent. Children born with thalassaemia major usually develop the symptoms of severe anaemia within the first year of life. Without regular treatment (blood transfusions and iron removal), death can occur.

**Thalassaemia minor:** Also known by the term “thalassaemia trait” or “carrier state”, it is a less serious form of the disorder referring to people who have genetic changes in one copy of the b-haemoglobin gene.

**Thrombophilia:** An inherited or acquired disorder that increases the risk of developing thrombosis (abnormal blood clotting) in the veins or arteries. Such an imbalance in the coagulation system results in a greater risk of clotting events, such as deep venous thrombosis (DVT), pulmonary embolism (PE) or stroke.
**Thrombocytopenia:** A condition characterized by abnormally low levels of thrombocytes, also known as “platelets”, in the blood. Patients may have splenomegaly and petechiae, as well as prolonged bleeding time.

**Thymine:** One of the four bases that make up DNA, abbreviated with a 'T'.

**Transfusion transmitted infections (TTIs):** A virus, parasite, or other potential pathogen that can be transmitted in donated blood through a transfusion to a recipient. Hepatitis C virus (HCV), Hepatitis B virus (HBV), human immunodeficiency virus (HIV), and syphilis are the most common infectious agents that may be transmitted via packed RCB transfusions.

**Ultrasound imaging:** A diagnostic medical procedure that uses high-frequency sound waves to produce dynamic visual images of organs, tissues or blood flow inside the body.

**Vaccination:** The administration of a vaccine to help the immune system develop protection from a disease. Vaccines contain a microorganism or virus in a weakened or killed state, or proteins or toxins from the organism. In stimulating the body’s adaptive immunity, they help prevent sickness from infectious diseases.
**Virus:** A small infectious agent that replicates only inside the living cells of an organism. Viruses can infect all types of life forms, from animals and plants to microorganisms, including bacteria.

**Vitamin:** A necessary micronutrient that an organism needs in small quantities for the proper functioning of its metabolism. Essential nutrients cannot be synthesized in the organism, either at all or not in sufficient quantities, and therefore must be obtained through the diet. A balanced daily regimen which includes vitamins such as C, D, E and B12, along with other antioxidants and minerals is highly recommended for patients with thalassaemia.

**Washed Red Cells:** They are red blood cells which have had most of the plasma, platelets and white blood cells removed and replaced with saline and another type of preservation solution. The most common reason for using washed red blood cells in transfusion medicine is to prevent the recurrence of severe allergic transfusion reactions that are caused by plasma proteins. The usual cause of these allergic reactions is proteins in the donor plasma. These proteins are removed by the process of washing the red blood cells.

**White Blood Cells (WBCs):** Also called “leucocytes”, they are the cells of the immune system that are involved in protecting the body against both infectious disease and foreign invaders such as bacteria, viruses, fungi and parasites. WBCs make up approximately 1% of the total blood volume in a healthy adult.