

Thalassemia

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THE STORY IN ONE SENTENCE

Thalassemia is a genetic failure to make enough of one type of hemoglobin chain, causing red blood cells to break apart too early and leading to lifelong anemia.

“Thalassemia is an inherited blood disorder where the body cannot make normal amounts of hemoglobin, the oxygen-carrying protein inside red blood cells. Because hemoglobin is defective or scarce, red blood cells die early, causing anemia that ranges from mild to life-threatening.”

Normal anatomy — the body's job

Red blood cells are made in the bone marrow and live about 120 days in the bloodstream. Each red blood cell is packed with hemoglobin, a protein made of four chains: two alpha-globin chains and two beta-globin chains. These chains wrap around iron-containing heme groups to pick up oxygen in the lungs and release it in tissues throughout the body.

BODY'S JOB

Hemoglobin works like a four-seat taxi balanced on both sides—two alpha drivers and two beta drivers—picking up oxygen passengers in the lungs and dropping them off wherever the body needs energy.

1. Bone marrow stem cells receive signals to become red blood cells
2. Developing red blood cells (erythroblasts) make equal amounts of alpha-globin and beta-globin protein chains
3. Two alpha chains and two beta chains combine with four heme-iron groups to form one complete hemoglobin molecule
4. Mature red blood cells filled with hemoglobin enter the bloodstream
5. Hemoglobin binds oxygen in the lungs and releases it in tissues
6. After 120 days, old red blood cells are removed by the spleen and recycled

What breaks

In thalassemia, one or more genes that tell the body how to make alpha or beta chains are deleted or broken. When alpha or beta chains are missing, the unpaired chains pile up inside developing red blood cells and form clumps that damage the cell membrane. These damaged cells die early in the bone marrow (ineffective erythropoiesis) or break apart soon after entering the bloodstream (hemolysis), leaving the body short of healthy red blood cells.

CLINICAL TERM

Thalassemia results from mutations or deletions in the HBA1, HBA2 (alpha-globin), or HBB (beta-globin) genes on chromosomes 16 or 11. Imbalanced globin-chain synthesis causes precipitation (clumping) of unpaired chains, forming insoluble aggregates that damage red cell membranes and organelles. This leads to ineffective erythropoiesis (death of red cell precursors in the marrow) and shortened red blood cell survival through red blood cell destruction (hemolysis) (early destruction in the spleen).

How the body compensates

The body senses low oxygen delivery and tries to make more red blood cells by releasing erythropoietin (EPO) from the kidneys, which drives the bone marrow to expand dramatically. The spleen and liver enlarge to clear damaged red cells and to help make new blood cells outside the marrow (extramedullary hematopoiesis), but these efforts cannot keep up with the rapid destruction.

1. {'step': 'Kidneys detect low oxygen and release erythropoietin (EPO)', 'detail': 'EPO is a hormone that tells bone marrow to make more red blood cells faster'}
2. {'step': 'Bone marrow expands into cortical bone', 'detail': '"Marrow spaces grow into skull, face, and long bones, causing thinning and deformities like 'chipmunk facies' and 'hair-on-end' appearance on X-ray'}
3. {'step': 'Extramedullary hematopoiesis begins', 'detail': 'Liver and spleen start making red blood cells outside the marrow, leading to an enlarged liver and spleen (hepatosplenomegaly) (enlarged liver and spleen)'}
4. {'step': 'Increased gastrointestinal iron absorption', 'detail': 'The body absorbs more iron from food because it senses anemia, even though iron stores are already high from red cell breakdown'}
5. {'step': 'Spleen works overtime to remove defective red cells', 'detail': 'Massive splenic activity causes further enlargement, abdominal discomfort, and risk of rupture or hypersplenism (destroying even healthy blood cells)'}

6. {'step': 'Heart increases output to deliver oxygen', 'detail': 'The heart pumps faster and harder to compensate for fewer red cells, eventually leading to high-output heart failure if anemia is severe and chronic'}

Domino effect

1. Genetic mutation reduces or eliminates alpha-globin or beta-globin chain production — Without balanced chains, hemoglobin cannot form properly
2. Unpaired globin chains precipitate inside red cell precursors in bone marrow — Excess chains form toxic clumps that damage developing red blood cells
3. Ineffective erythropoiesis: many red cell precursors die before maturing — Damaged cells never leave the marrow, causing chronic anemia despite marrow expansion
4. Defective red cells that do reach the bloodstream hemolyze early — Rigid, damaged membranes are recognized and destroyed by the spleen within days to weeks
5. Chronic severe anemia triggers massive EPO release and marrow expansion — Body tries to compensate but marrow output is ineffective, causing bone thinning, fractures, and facial deformities
6. Extramedullary hematopoiesis and massive an enlarged liver and spleen (hepatosplenomegaly) develop — Liver and spleen take over blood production and removal, enlarging painfully and compressing nearby organs
7. Iron overload accumulates from increased absorption and repeated transfusions — Excess iron deposits in heart, liver, and endocrine glands, causing cardiomyopathy (heart muscle disease), cirrhosis (liver scarring), diabetes, and hypogonadism (low sex hormones)
8. End-organ failure: heart failure, liver cirrhosis, endocrine collapse, and early death — Untreated or undertreated iron toxicity and chronic anemia damage vital organs irreversibly

Symptoms · what the patient feels, and why

- Pale skin and pale mucous membranes (pallor): Low hemoglobin (oxygen-carrying protein in red blood cells) from abnormal globin chains that break down quickly reduces oxygen delivery to tissues
- Extreme tiredness and weakness (fatigue): Fewer healthy red blood cells mean less oxygen reaches muscles and organs, so the body feels exhausted
- Shortness of breath with activity: Low red blood cell count reduces oxygen-carrying capacity, so the lungs work harder to get enough oxygen during movement
- Yellowing of skin and eyes (jaundice): Abnormal red blood cells break down early, releasing bilirubin (yellow pigment from broken hemoglobin) faster than the liver can clear it

- Enlarged spleen (splenomegaly): The spleen traps and destroys defective red blood cells, becoming swollen from overwork and storing extra blood cells
- Bone pain and facial changes (frontal bossing, prominent cheekbones): Bone marrow expands to make more red blood cells to compensate for anemia, pushing outward on skull and facial bones
- Slow growth and delayed puberty in children: Chronic anemia diverts energy away from normal growth, and iron overload from repeated transfusions damages endocrine glands
- Severe chest pain or sudden difficulty breathing: Can signal acute chest syndrome (lungs not getting oxygen), heart failure from chronic anemia, or pulmonary high blood pressure (hypertension) (high pressure in lung arteries)

Focused exam

- Conjunctival pale skin (pallor) (pale inner eyelids) and pale nail beds: Direct sign of anemia; severity of pale skin (pallor) roughly correlates with hemoglobin level
- Yellowing of the skin and eyes (Jaundice) in sclera (whites of eyes) and skin: Indicates ongoing red blood cell destruction (hemolysis) (red cell breakdown) with elevated indirect bilirubin
- An enlarged spleen (Splenomegaly) on abdominal examining by touch (palpation) (enlarged spleen felt below left rib cage): Shows extramedullary hematopoiesis (blood-cell production outside bone marrow) and increased red cell destruction; massive an enlarged spleen (splenomegaly) may need splenectomy
- An enlarged liver (Hepatomegaly) (enlarged liver) on abdominal exam: Suggests iron overload (hemosiderosis), extramedullary hematopoiesis, or chronic liver damage from transfusions or hepatitis C
- A fast heart rate (Tachycardia) (fast heart rate), heart murmur, or signs of heart failure (leg swelling, jugular vein distention): Chronic anemia forces the heart to pump harder; iron overload can cause restrictive cardiomyopathy and arrhythmias (irregular heartbeats)
- Frontal bossing, maxillary prominence, or pathologic fractures: Bone marrow expansion from chronic anemia causes facial deformities and weak bones prone to breaking

Diagnostics · every test answers a question

- Complete blood count (CBC) with red cell indices → How low is the hemoglobin, and what do the red blood cell size and number tell us about the anemia type?
- Peripheral blood smear microscopy → What do the red blood cells look like under the microscope?

- Hemoglobin electrophoresis or high-performance liquid chromatography (HPLC) → Which types of hemoglobin are present and in what amounts?
- Serum ferritin → Does the patient have iron overload from repeated transfusions or increased gut iron absorption?
- Liver function tests (ALT, AST, bilirubin) → Is the liver damaged from iron overload, chronic hepatitis, or red blood cell destruction (hemolysis)?
- Cardiac MRI (T2-star imaging) → How much iron has deposited in the heart muscle?
- Genetic testing (DNA analysis for globin gene mutations) → Which specific mutations or deletions are causing the thalassemia?
- Reticulocyte count → Is the bone marrow responding appropriately by making new red blood cells?

Treatment logic

- Regular red blood cell transfusions (every 2-4 weeks for beta-thalassemia major) → Replaces defective red cells with healthy donor cells, raises hemoglobin to near-normal (9-10.5 g/dL), suppresses ineffective bone marrow expansion, prevents bone deformities and growth delay
- Iron chelation therapy (removing excess iron with medication) → Binds iron in the blood and tissues so kidneys or intestines can remove it, prevents or reverses damage to heart, liver, and endocrine glands from hemosiderosis
- Folic acid supplementation (1 mg daily) → Supports red blood cell production because chronic red blood cell destruction (hemolysis) and bone marrow hyperactivity use up folate (vitamin needed for DNA synthesis) quickly
- Splenectomy (surgical removal of the spleen) → Reduces destruction of red blood cells, lowers transfusion frequency, and relieves abdominal discomfort from massive an enlarged spleen (splenomegaly)
- Hematopoietic stem cell transplant (bone marrow transplant) → Only curative treatment; replaces defective bone marrow with healthy donor marrow that makes normal red blood cells, eliminates need for transfusions and chelation
- Immunizations and antibiotic prevention (prophylaxis) post-splenectomy → Prevents life-threatening encapsulated bacterial infections in patients without functioning spleens; vaccines (pneumococcal, meningococcal, Haemophilus influenzae type b) and daily penicillin reduce infection risk

Medications

deferasirox · oral iron chelator

Deferasirox is a molecule that wraps around iron atoms in the bloodstream and tissues. The drug-iron complex then travels to the kidneys, which filter it out into urine. This removes excess iron that builds up from repeated blood transfusions.

1. Patient swallows tablet that dissolves in the stomach
2. Drug absorbs into bloodstream and spreads throughout body tissues
3. Deferasirox binds to free iron atoms (chelation), forming a stable complex
4. Kidneys filter the drug-iron complex from blood
5. Complex exits body in urine, lowering total body iron stores over months of daily use

SAFETY WATCH

Monitor kidney function (creatinine) monthly; can cause acute kidney injury · Monitor liver enzymes; can worsen liver disease · Risk of gastrointestinal bleeding and ulcers · Avoid in patients with poor kidney function (creatinine clearance below 40 mL/min)

deferoxamine · parenteral (injectable or infused) iron chelator

Deferoxamine is given by slow injection under the skin or into a vein over many hours. It binds tightly to iron in the blood and tissues, especially in the heart and liver. The kidneys and liver then remove the iron-drug combination from the body.

1. Drug infused subcutaneously (under skin) via portable pump over 8-12 hours, usually at night
2. Deferoxamine enters bloodstream and distributes to iron-loaded organs
3. Each molecule binds one iron atom with very high affinity
4. Kidneys excrete iron-deferoxamine complex in urine (turns reddish-orange color)
5. Liver also removes some complex into bile; daily infusions gradually reduce organ iron levels

SAFETY WATCH

Monitor hearing and vision; can cause sensorineural hearing loss and retinal toxicity · Local skin reactions at infusion site (pain, redness, swelling) · Risk of Yersinia enterocolitica infections (bacteria that thrive on iron-chelator complexes) · Avoid in patients with severe kidney disease

deferiprone · oral iron chelator

Deferiprone is a small pill that absorbs quickly from the gut into the blood. It crosses into heart muscle very well and pulls iron out of cells where it has deposited. The liver processes the drug-iron complex and removes it in urine and stool.

1. Patient takes tablets three times daily by mouth
2. Drug rapidly absorbs from intestines into bloodstream within 1 hour
3. Deferiprone crosses cell membranes and chelates intracellular iron
4. Drug-iron complex moves back into bloodstream
5. Liver and kidneys eliminate the complex; repeated dosing lowers cardiac and liver iron over time

SAFETY WATCH

Monitor white blood cell count weekly; can cause agranulocytosis (dangerously low neutrophils), which is life-threatening · Risk of arthropathy (joint pain and swelling) · Can cause zinc deficiency with long-term use · Avoid in pregnancy (teratogenic risk)

luspatercept · erythroid maturation agent (red blood cell maturation promoter)

Luspatercept is a protein given by injection under the skin every three weeks. It blocks certain signals (TGF-beta superfamily ligands) that stop red blood cell precursors from maturing. By removing this brake, more immature red cells in the bone marrow develop into healthy functioning red blood cells.

1. Drug injected subcutaneously every 21 days
2. Luspatercept binds to specific growth factors (like GDF11 and activin) in bone marrow
3. These growth factors normally inhibit late-stage red blood cell maturation
4. By trapping the inhibitory signals, luspatercept allows erythroblasts (red cell precursors) to mature into reticulocytes
5. More reticulocytes become functional red blood cells, raising hemoglobin and reducing transfusion need

SAFETY WATCH

Monitor blood pressure; can cause high blood pressure (hypertension) · Risk of thromboembolic events (blood clots) especially in patients with pre-existing clotting risk · Bone pain is a common side effect · Headache and dizziness reported

packed red blood cell transfusion · blood product replacement therapy

Donated red blood cells from healthy individuals are given directly into the patient's vein over 2-4 hours. The transfused cells immediately increase oxygen-carrying capacity by raising hemoglobin. Regular transfusions keep hemoglobin high enough to suppress the patient's own abnormal red cell production in the bone marrow.

1. Donor red blood cells are matched to patient blood type and screened for infections
2. Units of packed red cells infused intravenously in hospital or clinic
3. Transfused cells circulate immediately, binding and delivering oxygen to tissues
4. Higher hemoglobin reduces strain on heart and suppresses bone marrow overactivity
5. Transfused cells survive about 120 days, then need replacement

SAFETY WATCH

Screen for transfusion reactions (fever, chills, shortness of breath during infusion) · Monitor ferritin regularly; chronic transfusions cause iron overload requiring chelation · Risk of transfusion-transmitted infections (hepatitis B, hepatitis C, HIV) is very low but not zero · Alloimmunization can make future blood matching difficult

folic acid · water-soluble B vitamin (vitamin B9)

Folic acid is a vitamin needed to make DNA in all dividing cells, including red blood cell precursors. In thalassemia, the bone marrow works overtime to produce red cells, using up folate quickly. Daily folic acid supplements keep folate levels normal so DNA synthesis and red cell production do not slow down further.

1. Patient swallows folic acid tablet daily
2. Vitamin absorbs in the small intestine (jejunum)
3. Folate enters bloodstream and travels to bone marrow
4. Inside red cell precursors, folate participates in making purines and thymidine (DNA building blocks)
5. Adequate folate allows bone marrow to produce red cells without additional deficiency-related damage

SAFETY WATCH

Very safe with minimal side effects · Can mask vitamin B12 deficiency (rare issue in thalassemia patients) · No significant drug interactions · Typical dose is 1 mg daily

Red flags

- Severe chest pain or sudden shortness of breath may indicate heart failure or acute chest syndrome
- High fever in a patient after splenectomy requires immediate antibiotics for possible overwhelming sepsis
- Sudden severe abdominal pain with rapid drop in hemoglobin suggests splenic sequestration crisis or rupture
- New irregular heartbeat or fainting may signal iron overload cardiomyopathy with dangerous arrhythmias

Nursing priorities

1. Monitor hemoglobin and hematocrit levels closely — Thalassemia causes chronic anemia (low red blood cells) due to defective hemoglobin production, requiring regular monitoring to guide transfusion decisions and prevent organ damage from low oxygen (hypoxia) (low oxygen).
2. Assess for signs of iron overload — Repeated blood transfusions and increased intestinal iron absorption lead to iron buildup in the heart, liver, and endocrine glands, causing organ failure if untreated.
3. Administer chelation therapy as prescribed — Chelators (medicines that bind iron) like deferasirox or deferoxamine remove excess iron from the body to prevent or reverse damage to vital organs.
4. Educate families about genetic counseling and inheritance patterns — Thalassemia is autosomal recessive (both parents must carry a gene), so family members need testing and counseling before having children to understand their risks.
5. Monitor growth and development in pediatric patients — Chronic anemia and iron overload delay puberty, stunt growth, and cause skeletal changes like frontal bossing (large forehead) and maxillary overgrowth (enlarged upper jaw) from bone marrow expansion.
6. Prevent and manage infections promptly — Splenectomy (surgical removal of the spleen) for hypersplenism (overactive spleen) and iron overload both increase infection risk, especially from encapsulated bacteria like *Streptococcus pneumoniae*.
7. Coordinate interdisciplinary care with hematology, endocrinology, and cardiology — Thalassemia affects multiple organ systems requiring specialist management of cardiac dysfunction, diabetes, hypothyroidism, and bone disease from iron deposits.
8. Support psychosocial needs and quality of life — Lifelong transfusions, daily chelation therapy, chronic illness burden, and visible physical changes cause anxiety, depression, and social isolation requiring mental health support.

Sources

- American Society of Hematology (ASH) guidelines on transfusion and iron chelation therapy in thalassemia major (2021)
- Thalassemia International Federation (TIF) Guidelines for the Management of Transfusion Dependent Thalassemia (2022)
- National Heart, Lung, and Blood Institute (NHLBI) Evidence-Based Management of Sickle Cell Disease and Thalassemia (2020)
- American Academy of Pediatrics (AAP) recommendations on genetic counseling and care coordination for hemoglobinopathies (2019)

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