

G6PD Deficiency

G6PD deficiency means red blood cells cannot protect themselves from oxidative stress, so they suddenly burst when exposed to certain triggers like fava beans, infections, or specific medications.

THE STORY IN ONE SENTENCE

G6PD deficiency means red blood cells cannot protect themselves from oxidative stress, so they suddenly burst when exposed to certain triggers like fava beans, infections, or specific medications.

“G6PD deficiency is an inherited enzyme problem that makes red blood cells fragile. When exposed to certain foods, drugs, or infections, these cells break apart suddenly, causing anemia and dark urine.”

Normal anatomy — the body's job

Red blood cells live about 120 days and constantly face oxidative stress (damage from unstable oxygen molecules). G6PD (glucose-6-phosphate dehydrogenase) is an enzyme inside red blood cells that powers a protective pathway. This enzyme helps make NADPH (a molecule that carries energy), which keeps glutathione (a powerful antioxidant) in its active form. Active glutathione neutralizes hydrogen peroxide and other oxidants, preventing damage to the cell membrane and hemoglobin.

BODY'S JOB

Think of G6PD as the battery that powers a red blood cell's air filter, constantly scrubbing out toxic fumes so the cell can keep delivering oxygen without falling apart.

1. Red blood cell uses glucose for energy through a side pathway called the pentose phosphate pathway.
2. G6PD enzyme converts glucose-6-phosphate into another molecule, creating NADPH in the process.
3. NADPH powers the enzyme glutathione reductase, which recharges glutathione back to its active form.

4. Active glutathione neutralizes hydrogen peroxide and other harmful oxidants that build up inside the cell.
5. This antioxidant shield protects hemoglobin (the oxygen-carrying protein) from damage.
6. Protected red blood cells maintain their flexible membrane and circulate safely for 120 days.

What breaks

People with G6PD deficiency inherit a gene that makes a weak or low-functioning version of the G6PD enzyme. When the red blood cell faces extra oxidative stress from infections, certain drugs, or foods like fava beans, the small amount of G6PD cannot keep up with demand. Without enough protective glutathione, hydrogen peroxide and other oxidants damage hemoglobin and the cell membrane, causing the red blood cells to burst open suddenly.

CLINICAL TERM

G6PD deficiency is an X-linked recessive disorder caused by mutations in the G6PD gene on the X chromosome. The deficient enzyme cannot generate adequate NADPH (nicotinamide adenine dinucleotide phosphate), leading to depletion of reduced glutathione. Oxidative injury denatures hemoglobin into Heinz bodies (clumps of damaged hemoglobin) and damages the red cell membrane, triggering intravascular and extravascular red blood cell destruction (hemolysis) (red blood cell breakdown).

How the body compensates

The body tries to compensate for sudden red blood cell loss by rapidly making new red blood cells in the bone marrow. Because older red blood cells have less G6PD activity than younger ones, the newly released reticulocytes (young red blood cells) have slightly better enzyme levels, which helps stop the red blood cell destruction (hemolysis) once the trigger is removed. The spleen and liver work overtime to clear damaged cells and recycle iron from broken hemoglobin.

1. {'step': 'Bone marrow detects anemia through low oxygen signals (erythropoietin release from kidneys).', 'detail': 'Kidneys sense decreased oxygen delivery and secrete erythropoietin (a hormone that stimulates red blood cell production).'}
2. {'step': 'Bone marrow accelerates red blood cell production (erythropoiesis) up to six to eight times normal rate.', 'detail': 'Stem cells in the bone marrow divide rapidly and release young red blood cells (reticulocytes) into circulation earlier than usual.'}
3. {'step': 'Reticulocytes appear in peripheral blood with higher G6PD activity than older cells.', 'detail': 'Young red blood cells have more G6PD enzyme, so they resist oxidative damage better and survive longer during the crisis.'}

4. {'step': 'Spleen traps and destroys red blood cells with Heinz bodies (extravascular red blood cell destruction (hemolysis)).', 'detail': 'Macrophages (specialized immune cells) in the spleen recognize and remove damaged red blood cells, breaking down hemoglobin into bilirubin.'}
5. {'step': 'Liver processes excess bilirubin (a yellow breakdown product of hemoglobin) and excretes it in bile.', 'detail': 'Conjugated bilirubin moves into the intestine, giving stool its color, but overload can cause yellowing of the skin and eyes (jaundice) (yellowing of skin and eyes).'}
6. {'step': 'Iron from destroyed hemoglobin is recycled by the liver and spleen for new red blood cell production.', 'detail': 'Hepcidin (a liver hormone) may rise to prevent excess iron absorption, protecting organs from iron overload.'}

Domino effect

1. Patient encounters oxidative trigger (infection, fava beans, sulfa drugs, antimalarials like primaquine, or other oxidant medications). — Trigger generates hydrogen peroxide and other reactive oxygen species inside red blood cells beyond normal baseline levels.
2. Deficient G6PD cannot produce enough NADPH to meet increased demand for antioxidant protection. — The weak or unstable enzyme is overwhelmed, and the pentose phosphate pathway cannot keep up with oxidative stress.
3. Glutathione remains in its oxidized (inactive) form because NADPH is depleted. — Glutathione reductase requires NADPH to convert oxidized glutathione back to its active reduced form.
4. Uncontrolled oxidants denature hemoglobin, forming Heinz bodies (clumps of precipitated hemoglobin attached to the cell membrane). — Oxidative damage unfolds hemoglobin proteins, causing them to clump and stick to the inside of the red blood cell membrane.
5. Red blood cells become rigid and fragile, rupturing in circulation (intravascular red blood cell destruction (hemolysis)) or getting trapped in the spleen (extravascular red blood cell destruction). — Damaged membranes lose flexibility and break apart, or macrophages in the spleen recognize Heinz bodies and destroy the cells.
6. Hemoglobin released into plasma is filtered by kidneys, causing hemoglobinuria (dark tea-colored urine) and risk of acute kidney injury. — Free hemoglobin is toxic to kidney tubules, and large amounts can clog the filtration system, reducing kidney function.
7. Rapid drop in hemoglobin leads to severe anemia with fatigue, pale skin (pallor), yellowing of the skin and eyes (jaundice) (from excess bilirubin), and sometimes acute destroying red blood cells (hemolytic) crisis requiring transfusion. — Massive red blood cell destruction outpaces bone marrow production, and oxygen delivery to tissues falls dangerously low.

- 8.** In extreme cases, severe red blood cell destruction (hemolysis) causes cardiovascular collapse, acute renal failure, and death if not recognized and treated promptly. — Profound anemia reduces oxygen delivery to the heart and brain, while hemoglobin breakdown products and kidney failure create a life-threatening metabolic crisis.

Symptoms · what the patient feels, and why

- Dark tea-colored or cola-colored urine: Hemoglobin (oxygen-carrying protein from broken red blood cells) spills into urine after acute red blood cell destruction (hemolysis) (rapid red blood cell destruction) triggered by oxidative stress
- Sudden fatigue and weakness: Anemia (low red blood cell count) reduces oxygen delivery to muscles and brain following destroying red blood cells (hemolytic) crisis (episode of rapid red blood cell breakdown)
- Pale skin and mucous membranes: Loss of hemoglobin-carrying red blood cells decreases the red color in skin and inside the mouth and eyelids during red blood cell destruction (hemolysis)
- Yellowing of eyes and skin (jaundice): Bilirubin (yellow breakdown product of hemoglobin) accumulates in blood and tissues when liver cannot process the large amount released during red blood cell destruction (hemolysis)
- Rapid heartbeat (tachycardia): Heart pumps faster to compensate for reduced oxygen-carrying capacity when red blood cell count drops suddenly
- Shortness of breath with activity: Decreased red blood cell mass cannot deliver adequate oxygen to working muscles during exertion, triggering air hunger
- Back pain or abdominal pain: Hemoglobin released from lysed (broken) red blood cells irritates kidney tubules or spleen capsule stretches from filtering damaged cells
- Fever during destroying red blood cells (hemolytic) episode: Released red blood cell contents and inflammatory cytokines (chemical messengers) trigger the body's temperature-regulation center during acute red blood cell destruction (hemolysis)

Focused exam

- Scleral yellowing of the eyes (icterus) (yellowing of the white part of eyes) and jaundiced skin: Indicates elevated unconjugated bilirubin (bilirubin not yet processed by liver) from ongoing red blood cell destruction (hemolysis) rather than liver disease
- Pale skin (Pallor) of conjunctiva (inside eyelids), palmar creases, and nail beds: Reflects degree of anemia and helps estimate severity of red blood cell loss before laboratory results are available

- A fast heart rate (Tachycardia) (heart rate above 100 beats per minute) and fast breathing (tachypnea) (breathing rate above 20 breaths per minute): Compensatory mechanisms for anemia that signal significant oxygen-carrying capacity loss and need for monitoring or transfusion consideration
- An enlarged spleen (Splenomegaly) (enlarged spleen felt below left rib cage): Spleen enlarges from working overtime to filter damaged red blood cells during chronic or repeated destroying red blood cells (hemolytic) episodes
- Altered mental status, confusion, or lethargy: Indicates severe anemia with inadequate cerebral oxygenation requiring immediate intervention and possible red blood cell transfusion
- Orthostatic vital signs (blood pressure drop and heart rate rise when standing): Suggests significant intravascular volume depletion or severe anemia affecting cardiovascular compensation and increases fall risk

Diagnostics · every test answers a question

- G6PD enzyme activity assay (quantitative level) → Does the patient have glucose-6-phosphate dehydrogenase deficiency and how severe is the enzyme reduction?
- Complete blood count (CBC) with reticulocyte count → How severe is the anemia and is the bone marrow responding appropriately by making new red blood cells?
- Peripheral blood smear → What specific red blood cell changes indicate red blood cell destruction (hemolysis) and rule out other causes of anemia?
- Lactate dehydrogenase (LDH) level → Is there evidence of active red blood cell breakdown releasing intracellular enzymes?
- Total and indirect (unconjugated) bilirubin → How much hemoglobin breakdown is occurring and is the liver processing it normally?
- Haptoglobin level → Is free hemoglobin circulating in the blood from intravascular red blood cell destruction (hemolysis) (cell breakdown inside blood vessels)?
- Urinalysis with microscopy → Is hemoglobin being filtered into urine and are kidneys being damaged?
- Basic metabolic panel (BMP) with creatinine → Are kidneys functioning normally or being injured by hemoglobin precipitation?

Treatment logic

- Immediate cessation of triggering agent (medication, food, or supplement) → Stops ongoing oxidative stress generation allowing remaining healthy red blood cells to survive and preventing further red blood cell destruction (hemolysis) within hours

- Intravenous hydration with normal saline or lactated Ringer solution → Maintains renal blood flow (perfusion) (kidney blood flow) and dilutes hemoglobin in tubules to prevent precipitation and acute kidney injury during destroying red blood cells (hemolytic) crisis
- Red blood cell transfusion for symptomatic anemia → Immediately increases oxygen-carrying capacity and hemoglobin level to relieve symptoms like chest pain, severe fatigue, or altered mental status
- Folic acid supplementation (1 mg daily during recovery) → Provides folate (vitamin needed for DNA synthesis) to support accelerated red blood cell production during bone marrow recovery from destroying red blood cells (hemolytic) episode
- Patient and family education on trigger avoidance → Prevents future destroying red blood cells (hemolytic) crises by teaching recognition of high-risk medications (sulfa drugs, antimalarials, aspirin, nitrofurantoin), foods (fava beans), and situations (infections requiring early treatment)
- Medical alert bracelet or wallet card listing G6PD deficiency → Ensures emergency providers and new clinicians avoid prescribing triggering medications during acute illness or when patient cannot communicate

Medications

Normal saline (0.9% sodium chloride IV fluid) · Isotonic crystalloid solution

This sterile salt water matches the salt concentration in blood. It expands blood volume and increases fluid flowing through kidneys. Higher kidney flow dilutes and flushes out hemoglobin before it can clump and block kidney tubules.

1. Isotonic fluid enters bloodstream without shifting water into or out of cells
2. Increased blood volume raises pressure in kidney glomeruli (filtering units)
3. Higher pressure increases glomerular filtration rate and urine flow
4. Faster tubular flow prevents hemoglobin concentration and precipitation
5. Diluted hemoglobin passes through tubules without forming obstructing casts

SAFETY WATCH

Monitor for fluid overload (lung crackles, leg swelling) in patients with heart failure or kidney disease · Check electrolytes as large volumes can cause hyperchloremic metabolic acidosis (acid building up in the blood) (high chloride, low bicarbonate) · Avoid in patients with severe high sodium (hypernatremia) (high sodium) or fluid overload · Reassess volume status frequently during rapid administration

Packed red blood cells (PRBC transfusion) · Blood product replacement therapy

These are concentrated red blood cells from donated blood with most plasma removed. Each unit contains normal G6PD enzyme and hemoglobin. Transfused cells immediately carry oxygen to tissues and organs that are suffering from low oxygen delivery during severe anemia.

1. Donor red blood cells with normal hemoglobin enter patient circulation through IV
2. New cells increase total red blood cell mass and hemoglobin concentration within minutes
3. Higher hemoglobin increases blood oxygen-carrying capacity immediately
4. Improved oxygen delivery relieves tissue low oxygen (hypoxia) (low oxygen) in heart, brain, and muscles
5. Transfused cells survive normally (120 days) unless oxidative trigger continues

SAFETY WATCH

Monitor for transfusion reactions (fever, chills, back pain, hives, breathing difficulty) especially in first 15 minutes · Check blood type compatibility before starting transfusion to prevent destroying red blood cells (hemolytic) reaction · Watch for fluid overload in elderly or heart failure patients; give furosemide between units if needed · Transfuse slowly (2-4 hours per unit) unless life-threatening bleeding (hemorrhage)

Folic acid (folate) · Water-soluble B-vitamin supplement

Folic acid is a vitamin that bone marrow needs to build DNA in new red blood cells. During red blood cell destruction (hemolysis) the marrow works overtime making replacement cells and uses up folate stores quickly. Supplementing folate ensures the marrow has enough raw material to maintain high red blood cell production rates.

1. Oral folic acid absorbs in small intestine and enters bloodstream
2. Liver converts folate to active form tetrahydrofolate (THF)
3. THF travels to bone marrow and enters red blood cell precursors
4. THF donates one-carbon units needed for DNA base synthesis (purines and thymidine)
5. Adequate DNA synthesis allows marrow to maintain accelerated red blood cell production during recovery

SAFETY WATCH

Check vitamin B12 level before starting as folate can mask B12 deficiency anemia while allowing nerve damage to progress · High doses (above 5 mg daily) may interact with antiseizure medications · Generally very safe with rare side effects · Not urgent therapy; used during recovery phase not acute crisis

Supplemental oxygen therapy · Medical gas therapy

Increasing oxygen concentration in inhaled air raises oxygen levels dissolved in blood plasma (liquid part). This improves oxygen delivery to tissues even when red blood cell count is low. Higher oxygen partial pressure helps remaining healthy red blood cells load more oxygen molecules onto their hemoglobin.

1. Higher oxygen concentration in lungs increases alveolar oxygen partial pressure
2. More oxygen dissolves in blood plasma following concentration gradient
3. Increased dissolved oxygen and higher hemoglobin saturation improve arterial oxygen content
4. Better-oxygenated blood delivers more oxygen per circulation cycle to tissues
5. Temporarily compensates for reduced oxygen-carrying capacity from anemia

SAFETY WATCH

Titrate to oxygen saturation 92-96% in most patients; avoid hyperoxia (too much oxygen) · Use lower saturation targets (88-92%) in patients with chronic lung disease · Oxygen supports combustion so keep away from open flames and electrical sparks · Prolonged high concentrations (above 60%) can cause oxygen toxicity with lung damage

Acetaminophen (for fever or pain management) · Non-opioid analgesic and antipyretic

Acetaminophen reduces fever by acting on the brain's temperature-control center and relieves pain by blocking pain signals in the brain and spinal cord. It does not cause oxidative stress like aspirin or NSAIDs. Safe pain and fever control is important because fever increases metabolic demands and many pain medications trigger red blood cell destruction (hemolysis) in G6PD deficiency.

1. Acetaminophen absorbs from stomach and enters bloodstream
2. Drug crosses blood-brain barrier to reach hypothalamus
3. Inhibits cyclooxygenase (COX) enzymes in brain reducing prostaglandin E2 (fever-causing chemical)
4. Lowers hypothalamic temperature set-point back to normal triggering heat loss

5. Also blocks pain perception in spinal cord reducing discomfort signals

SAFETY WATCH

Maximum adult dose 3 grams per 24 hours (4 grams only under physician supervision) to prevent liver toxicity · Avoid in patients with severe liver disease or active alcohol use disorder · Check all other medications for hidden acetaminophen to prevent accidental overdose · Unlike aspirin and NSAIDs, acetaminophen is safe in G6PD deficiency at therapeutic doses

Infection treatment (pathogen-specific antimicrobials when indicated) · Varies by pathogen (antibiotics, antivirals, or antifungals)

Infections generate oxidative stress that triggers red blood cell destruction (hemolysis) in G6PD-deficient patients. Treating the infection reduces inflammatory cytokines (chemical signals) and oxidative free radicals. Lower oxidative stress allows remaining red blood cells to survive and stops ongoing red blood cell destruction. Must choose infection treatments that do not themselves trigger red blood cell destruction.

1. Antimicrobial kills or inhibits growth of causative pathogen
2. Reduced pathogen burden decreases immune system activation
3. Lower cytokine production reduces systemic oxidative stress generation
4. Decreased oxidative stress prevents further red blood cell membrane damage
5. Remaining healthy red blood cells survive allowing hemoglobin stabilization

SAFETY WATCH

Avoid sulfonamides (sulfamethoxazole-trimethoprim, sulfasalazine) which trigger severe red blood cell destruction (hemolysis) in G6PD deficiency · Avoid nitrofurantoin, dapsone, and quinolone antibiotics (ciprofloxacin, levofloxacin) as they cause oxidative stress · Choose penicillins, cephalosporins, or azithromycin when appropriate for infection type · Consult pharmacy or reference guide for G6PD-safe alternatives before prescribing

Red flags

- Dark tea-colored urine with decreased urine output suggests acute kidney injury from hemoglobin precipitation requiring immediate IV hydration
- Chest pain, severe shortness of breath, confusion, or altered mental status indicates life-threatening anemia needing urgent transfusion
- Hemoglobin below 7 g/dL with ongoing red blood cell destruction (hemolysis) requires hospital admission and transfusion consideration

- Recent exposure to triggering medications (sulfa drugs, antimalarials, aspirin, nitrofurantoin) or fava beans with symptoms starting within 24-72 hours

Nursing priorities

1. Screen for recent triggers (infection, fava beans, medications) that may have caused red blood cell destruction (hemolysis) (red blood cell breakdown). — G6PD deficiency causes red blood cells to break apart when exposed to oxidative stress (cell damage from certain triggers). Identifying the trigger helps prevent further red blood cell destruction (hemolysis) and guides treatment.
2. Monitor for signs of acute destroying red blood cells (hemolytic) crisis: dark tea-colored urine, yellowing of the skin and eyes (jaundice) (yellow skin), fatigue, rapid heart rate, and shortness of breath. — Destroying red blood cells (Hemolytic) crisis can happen suddenly when many red blood cells break down at once. This releases hemoglobin (oxygen-carrying protein) into the blood and urine, causing organ damage if not caught early.
3. Check baseline and serial complete blood count (CBC) focusing on hemoglobin, hematocrit, and reticulocyte count (young red blood cells). — Hemoglobin drops during red blood cell destruction (hemolysis) show how severe the crisis is. Reticulocyte count rising means the bone marrow is responding by making new red blood cells. Serial checks track if red blood cell destruction is worsening or improving.
4. Assess for signs of severe anemia: pale skin and mucous membranes, dizziness, chest pain, confusion, and decreased urine output. — Severe anemia means not enough oxygen reaches vital organs. The heart, brain, and kidneys are most at risk. Early recognition allows for oxygen support and possible blood transfusion.
5. Educate the patient and family about avoiding known oxidative triggers including certain medications, foods, and infections. — Prevention is the main treatment for G6PD deficiency. Common triggers include sulfa drugs, aspirin, fava beans, naphthalene (mothballs), and infections. Avoiding triggers prevents future destroying red blood cells (hemolytic) episodes.
6. Ensure adequate hydration with IV fluids during destroying red blood cells (hemolytic) crisis to protect kidney function. — When red blood cells break down, free hemoglobin can block kidney tubules (small filtering tubes) and cause acute kidney injury. Good urine flow helps flush hemoglobin through the kidneys safely.
7. Review the medication list and alert providers to stop any oxidizing drugs immediately. — Continuing the offending medication will cause ongoing red blood cell destruction (hemolysis). Common culprits include trimethoprim-sulfamethoxazole, dapsone, primaquine, nitrofurantoin, and rasburicase. Stopping the trigger is urgent.

8. Prepare for possible blood transfusion if hemoglobin falls below 7 g/dL or patient shows signs of cardiovascular compromise. — Severe anemia with symptoms like chest pain, confusion, or heart failure needs emergency red blood cell transfusion. Transfusion quickly restores oxygen delivery to vital organs while the body recovers.

Sources

- American Society of Hematology (ASH) guidelines on diagnosis and management of glucose-6-phosphate dehydrogenase deficiency, 2020
- Centers for Disease Control and Prevention (CDC) recommendations for G6PD testing and prevention of drug-induced hemolysis, 2021
- National Institutes of Health (NIH) Genetic and Rare Diseases Information Center G6PD deficiency clinical overview, 2022
- American Academy of Pediatrics (AAP) guidelines on screening and management of G6PD deficiency in newborns and children, 2019

Last reviewed: 2026-08-29