

G6PD Deficiency

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.

THE ONE-LINE TRUTH

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 chain — how it unfolds

1. Patient encounters oxidative trigger (infection, fava beans, sulfa drugs, antimalarials like primaquine, or other oxidant medications). — why: 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. — why: 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. — why: 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). — why: 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). — why: 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. — why: 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. — why: 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. — why: Profound anemia reduces oxygen delivery to the heart and brain, while hemoglobin breakdown products and kidney failure create a life-threatening metabolic crisis.

Spot it — what you see, 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

Red flags — act now

- 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

Treat it — in this order

1. 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
2. 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
3. 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
4. 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
5. 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)

Your top priorities at the bedside

1. Screen for recent triggers (infection, fava beans, medications) that may have caused red blood cell destruction (hemolysis) (red blood cell breakdown). — why: 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. — why: 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). — why: 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.