

Iron Deficiency Anemia

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THE STORY IN ONE SENTENCE

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“In adults with iron deficiency anemia, always hunt for the bleeding source — usually the gut in older adults, periods in younger women — then replace the iron.”

Normal anatomy — the body's job

Iron moves through the body in a careful cycle: you absorb it from food in the duodenum, store extras as ferritin in the liver, build it into hemoglobin inside red blood cells in the bone marrow, and recycle most of it when old red blood cells die after about 120 days.

BODY'S JOB

Iron's main job is to sit in the middle of hemoglobin molecules inside red blood cells and grab oxygen in the lungs, then release it in tissues that need it. The body holds about 3–4 grams of total iron: roughly two-thirds is in circulating hemoglobin, one-quarter is stored as ferritin, and a small amount circulates bound to transferrin (the taxi protein that shuttles iron from gut to bone marrow). Because the body has no active way to dump excess iron, it tightly controls absorption — the duodenum absorbs only about 1–2 mg per day from food to replace the tiny amount lost in dead skin and gut cells. Most iron is recycled: macrophages (cleanup white blood cells) in the spleen and liver eat old red blood cells, pull out the iron, and send it back to the bone marrow to build new hemoglobin. This cycle keeps iron supply steady without needing much new iron from food.

1. You eat iron-rich food (meat, beans, fortified cereal); stomach acid helps release iron from the food.
2. The duodenum (first part of the small intestine) absorbs iron through special transporter proteins in its lining cells and releases it into the bloodstream.

3. Transferrin (a carrier protein made by the liver) picks up iron in the blood and ferries it to the bone marrow.
4. In the bone marrow, developing red blood cells grab iron from transferrin and build it into hemoglobin molecules.
5. Mature red blood cells packed with hemoglobin leave the marrow, circulate for about 120 days, pick up oxygen in the lungs, and deliver it to every tissue.
6. When red blood cells age and die, macrophages in the spleen and liver break them down, reclaim the iron, and send it back into the bloodstream bound to transferrin — restarting the cycle.
7. Any extra iron is stored as ferritin in the liver, ready to be mobilized if absorption drops or demand spikes.

What breaks

Iron deficiency anemia happens when iron leaves the body faster than it comes in, or when the gut cannot absorb it properly, or when the body suddenly needs much more than usual.

CLINICAL TERM

The upstream break is negative iron balance: blood loss (chronic GI bleeding from ulcer, gastritis, colon polyp or cancer in older adults; heavy menstrual bleeding in premenopausal women), malabsorption (celiac disease, atrophic gastritis, *H. pylori* infection, or post-gastrectomy), inadequate dietary intake (strict vegan diet without supplementation, poverty, eating disorders), or increased physiologic demand (pregnancy, rapid growth in adolescence, frequent blood donation). Blood loss is by far the most common cause in adults.

How the body compensates

The body can hide early iron loss by draining storage iron (ferritin) first, keeping hemoglobin normal for months — so vital signs and hemoglobin may look fine even while iron stores are already empty. By the time anemia appears, the bleeding or malabsorption has been going on for a long time. The danger is missing the hidden bleeding source (especially colon cancer) during this silent window.

1. In the first weeks to months of negative iron balance, the body pulls from ferritin stores in the liver — serum ferritin drops but hemoglobin and MCV stay normal, so the patient feels fine and no anemia shows on a CBC.

2. Once ferritin is depleted, serum iron falls and transferrin (the iron taxi) rises trying to capture any iron — transferrin saturation drops below 20%, but hemoglobin may still be near-normal because the marrow can still recycle iron from dying red cells.
3. After several more months, the bone marrow cannot make enough hemoglobin, so new red cells come out small (MCV starts dropping below 80 fL) and pale, and hemoglobin finally falls — the patient now has microcytic anemia and starts feeling tired, but vital signs (heart rate, blood pressure) are often still normal at rest because anemia developed slowly and the body adapted.
4. The heart compensates by beating faster (mild a fast heart rate (tachycardia)) and pumping harder (increased stroke volume and cardiac output) to deliver the same amount of oxygen with fewer red cells — blood pressure stays normal, so the patient and clinician may underestimate severity.
5. The body shunts blood to vital organs (brain, heart, kidneys), so skin and mucous membranes look pale (pallor) — this is not dangerous itself, just a visible marker of low hemoglobin.
6. Chronic low oxygen in tissues triggers bizarre compensations: nails become thin and spoon-shaped (koilonychia) because the nail bed is starved for oxygen; the brain's dopamine pathways misfire (low iron is a cofactor for dopamine synthesis) causing restless legs syndrome; and the hypothalamus drives cravings for ice, dirt, or starch (pica) in a confused attempt to find minerals — none of these help, but they signal severe, prolonged deficiency.
7. The dangerous middle: the patient looks stable (normal blood pressure, mild symptoms) but is sitting on months of hidden bleeding — if the source is colon cancer, this delay lets the tumor grow and spread. Always investigate the bleeding source in adults before simply replacing iron.
8. The crash point to watch: if bleeding continues or iron is not replaced, hemoglobin eventually drops so low ($< 7\text{--}8$ g/dL) that the heart cannot compensate anymore — high-output heart failure, severe fatigue, fainting (syncope), angina (if coronary disease present), and even heart attack can occur, especially in older adults. Once you reach this point, recovery is slower and riskier.

Domino effect

1. Iron leaves the body faster than it comes in — chronic slow bleeding (hidden ulcer, colon polyp or cancer, heavy periods), poor gut absorption (celiac disease, low stomach acid), or inadequate diet. — The body loses 2–5 mg of iron per day from bleeding or malabsorption, but can only absorb 1–2 mg per day from food, so iron balance tips negative and stores begin to drain.

2. Ferritin (stored iron in the liver) drops first, often below 15–30 ng/mL, while hemoglobin is still normal — this is the silent phase. — The body sacrifices storage iron to keep circulating red cells normal as long as possible; serum ferritin is the earliest lab marker of iron deficiency, dropping months before anemia appears.
3. Once ferritin is empty, serum iron falls, transferrin rises (high TIBC), and transferrin saturation drops below 20% — the marrow is now starved for iron. — With no storage iron left, the liver makes extra transferrin (the iron shuttle protein) trying to scavenge any available iron, but there is none to find — so transferrin circulates mostly empty (low saturation).
4. The bone marrow cannot build normal hemoglobin anymore, so new red blood cells come out small (microcytic, $MCV < 80$ fL) and pale (hypochromic, low MCHC) — hemoglobin finally starts to drop. — Hemoglobin needs iron at its core to grab oxygen; without iron, red cell precursors divide one extra time trying to keep total hemoglobin per cell adequate, producing smaller, paler cells that carry less oxygen — this is microcytic hypochromic anemia.
5. Tissues and organs do not get enough oxygen, so the patient feels exhausted, weak, short of breath with exertion, dizzy, and has trouble concentrating (brain fog). — Every cell in the body depends on oxygen to make energy (ATP); with fewer red cells and less hemoglobin, oxygen delivery falls, so muscles tire quickly and the brain slows down — fatigue is the hallmark symptom.
6. The heart tries to compensate by beating faster (tachycardia) and pumping harder (increased cardiac output) to push what little oxygen is available around the body faster. — The heart senses low oxygen delivery (via chemoreceptors and reduced oxygen content in blood) and increases rate and stroke volume to keep oxygen delivery near normal — this works for a while but eventually exhausts the heart if anemia is severe or prolonged.
7. Skin and mucous membranes look pale (pallor), especially the conjunctiva (inside lower eyelid), palms, and nail beds, because blood is shunted to vital organs and hemoglobin is low. — Pale skin is a direct result of less hemoglobin (the red pigment in blood) and vasoconstriction in non-essential areas — it is a visible clue that anemia is present.
8. Fingernails become thin, brittle, and spoon-shaped (koilonychia) with the center dipping inward; the tongue may become smooth, red, and sore (atrophic glossitis); and cracks appear at the corners of the mouth (angular cheilitis). — Chronic low oxygen and iron deficiency in rapidly dividing cells (nails, tongue lining, mouth corners) cause abnormal growth — koilonychia and glossitis are specific physical exam signs of long-standing severe iron deficiency.

9. The patient craves and chews ice (pagophagia), dirt, clay, or raw starch (pica) — bizarre non-food cravings that signal severe iron deficiency. — The exact mechanism is unknown, but the hypothalamus (the brain's control center for hunger and cravings) and dopamine pathways (which need iron as a cofactor) misfire in severe iron deficiency, driving cravings for non-nutritive substances — pica often resolves within days of starting iron replacement.
10. Legs feel restless and uncomfortable at night, with an irresistible urge to move them (restless legs syndrome), disrupting sleep. — Iron is a cofactor for tyrosine hydroxylase, the enzyme that makes dopamine in the brain; low iron disrupts dopamine signaling in the basal ganglia (the brain region that controls smooth movement), causing restless legs — this improves with iron repletion even before anemia fully corrects.
11. If bleeding continues and anemia worsens (hemoglobin drops below 7–8 g/dL), the heart can no longer compensate — high-output heart failure, fainting (syncope), angina, or even heart attack (myocardial infarction) can occur, especially in older adults with underlying heart disease. — Severe anemia forces the heart to pump much harder and faster for months, eventually exhausting the myocardium (heart muscle); in patients with coronary artery disease, the combination of increased oxygen demand by the heart and decreased oxygen delivery by anemic blood can trigger angina or heart attack — this is the life-threatening crash point.

Symptoms · what the patient feels, and why

- Feeling very tired and weak all the time: Your red blood cells carry oxygen around your body using iron. When you don't have enough iron, you can't make enough hemoglobin (the oxygen-carrying part of red blood cells), so less oxygen reaches your muscles and brain. It's like trying to run a car on half a tank — everything slows down.
- Pale skin, especially inside the eyelids, under the nails, and on the palms: Hemoglobin gives blood its red color. When you don't have enough hemoglobin because of low iron, your blood looks lighter and your skin loses its usual pink tone — especially in thin-skinned spots where blood vessels show through.
- Shortness of breath, especially when active: Your body isn't getting enough oxygen from your low red blood cell count, so your lungs try to work harder to pull in more air. Even small efforts like climbing stairs can leave you winded because your blood can't deliver enough oxygen to keep up with what your muscles need.
- Fast or pounding heartbeat: Your heart speeds up to pump blood faster, trying to deliver enough oxygen even though each red blood cell is carrying less than normal. It's like your heart is racing to make up for weaker fuel.

- **Headaches and trouble concentrating or remembering things:** Your brain uses about 20% of your body's oxygen. When iron is low and oxygen delivery drops, the brain doesn't get the fuel it needs to focus, remember, and think clearly — you might feel foggy or get dull, throbbing headaches.
- **Cold hands and feet:** Your body sends blood to your most important organs first (like your heart and brain) when oxygen is tight. That means less warm blood reaches your fingers and toes, so they feel cold even in a warm room.
- **Craving ice or non-food items like dirt or starch (called pica):** Scientists don't fully understand why, but severe iron deficiency can change how your brain signals cravings. It may involve changes in dopamine (a brain messenger that controls reward and motivation) when iron is very low. This craving usually goes away once iron levels come back up.
- **Sore, smooth, or swollen tongue:** The cells in your tongue turn over quickly and need iron to grow. When iron runs low, these cells can't renew properly, so the tongue loses its normal bumpy texture (called papillae) and can become smooth, red, and tender.
- **Brittle nails that crack or spoon inward (koilonychia):** Nails need iron to build strong keratin (the tough protein that forms the nail). Without enough iron, nails grow thin and weak, and in severe cases the edges can curl up like a spoon.
- **Lab results showing small, pale red blood cells (microcytic hypochromic anemia), low ferritin (the body's iron storage protein — most specific test), low serum iron, and high TIBC (total iron-binding capacity, meaning your blood is hungry for iron):** Your bone marrow can't build normal-sized red blood cells without enough iron, so the cells come out smaller (microcytic) and paler (hypochromic) than usual. Ferritin drops early because your body drains its iron stores first. TIBC goes up because your blood makes extra transferrin (the carrier protein for iron), trying to grab any iron it can find — like sending out more trucks when supplies are running low.

Focused exam

- **Pale conjunctiva (inside of eyelids) and pale nail beds:** When iron deficiency shrinks the number of red blood cells, less hemoglobin flows through tiny blood vessels, so the usual pink color fades. Pale conjunctiva and nail beds are your first visual clue that oxygen carriers are low.
- **Spoon nails (koilonychia) — nails flatten and curl upward like spoons:** Iron is needed to build strong nail cells. When iron stores run empty for weeks to months, the nail bed weakens and the nail curls up. This finding tells you the iron deficiency has been going on for a while, not just days.
- **Glossitis — swollen, smooth, red tongue that may feel sore:** The tongue surface renews itself quickly and needs iron to build new cells. Chronic iron deficiency damages the tongue lining, flattening the bumps (papillae) and leaving a bald, red, sore tongue.

- Pica — craving and eating ice, dirt, clay, or starch: Iron deficiency disrupts dopamine signaling in the striatum (the brain's movement and reward center), triggering strange cravings. Pica is a red flag for severe or long-standing iron lack.
- A fast heart rate (Tachycardia) (fast heart rate) at rest or mild exertion, and a soft systolic flow murmur: When red blood cells drop, the heart pumps faster to deliver the same oxygen. Thin, watery blood flows turbulently through the valves, creating a murmur. Together these findings mean the anemia is severe enough to stress the heart.
- Black, tarry stool (melena), visible blood in stool, or guaiac-positive (hidden blood) on stool test: In adults, especially men and postmenopausal women, gastrointestinal bleeding is the most common cause of iron deficiency. Finding blood in the stool means you have located the upstream source of iron loss.

Diagnostics · every test answers a question

- Complete blood count (CBC) with red cell indices → Is the patient anemic, and are the red blood cells small (microcytic)?
- Serum ferritin → How much iron is stored in the body?
- Serum iron and total iron-binding capacity (TIBC), calculated as transferrin saturation → How much iron is circulating in the blood, and how much capacity is left to carry more?
- Reticulocyte count → Is the bone marrow trying to make new red blood cells?
- Fecal occult blood test (FOBT) or fecal immunochemical test (FIT) → Is there hidden bleeding in the gastrointestinal tract?
- Upper endoscopy (esophagogastroduodenoscopy) and colonoscopy → Where is the GI tract bleeding?
- Tissue transglutaminase IgA (tTG-IgA) with total IgA, or celiac serology panel → Is celiac disease blocking iron absorption in the duodenum?
- Hemoglobin electrophoresis (if MCV low but ferritin normal) → Could this be thalassemia trait instead of iron deficiency?

Treatment logic

- Identify and treat the source: colonoscopy and upper endoscopy in men and postmenopausal women; address heavy menstrual bleeding in premenopausal women; screen for celiac disease if malabsorption suspected → Stops the upstream leak or blockage so the body can rebuild iron stores instead of losing iron faster than you can replace it. Treating a bleeding ulcer, polyp, or menstrual disorder is the only way to truly fix iron deficiency anemia.

- Oral ferrous sulfate 325 mg (65 mg elemental iron) every other day on an empty stomach, or ferrous gluconate or ferrous fumarate at equivalent elemental iron dose → Delivers iron to the duodenum (first part of the small intestine), where the body absorbs it and shuttles it to the bone marrow to make hemoglobin. Every-other-day dosing improves absorption and cuts side effects like nausea and constipation.
- Intravenous iron: ferric carboxymaltose 750–1000 mg, iron sucrose 200 mg, or low-molecular-weight iron dextran, if oral fails, malabsorption present, severe anemia (hemoglobin < 10 g/dL), inflammatory bowel disease, chronic kidney disease, or pregnancy → Bypasses the intestine and delivers iron directly into the bloodstream, filling the body's iron tank even when the gut cannot absorb pills. IV iron works faster and replenishes stores in days to weeks instead of months.
- Recheck hemoglobin at 4 weeks, then every 8 weeks until normal; recheck ferritin at 3 months to confirm iron stores are replenished (goal ferritin > 50–100 ng/mL) → Confirms the iron is being absorbed and used to make new red blood cells. Hemoglobin should rise 1–2 g/dL per month. Ferritin tells you whether the body's iron tank is refilling or still empty.
- Vitamin C 200 mg with oral iron to boost absorption (optional, not required) → Vitamin C (ascorbic acid) keeps iron in the ferrous (Fe^{2+}) form, which is absorbed better in the duodenum. May speed iron repletion slightly.
- Blood transfusion: packed red blood cells, 1–2 units, if hemoglobin < 7 g/dL with symptoms (severe fatigue, chest pain, shortness of breath) or < 8 g/dL with active bleeding or heart disease → Instantly raises hemoglobin by 1 g/dL per unit, restoring oxygen delivery to tissues within hours. Buys time while iron replacement catches up.

Medications

Ferrous sulfate (oral iron) · Oral iron supplement

Ferrous sulfate gives your body iron—the metal your bone marrow needs to build hemoglobin (the oxygen-carrying protein inside red blood cells). When you don't have enough iron, your marrow can't make enough hemoglobin, so your red cells stay small and pale and can't carry enough oxygen. Taking iron every other day (rather than every day) actually helps your gut absorb more of each dose and causes less nausea, because your gut lining needs a day to reset its iron-import machinery.

1. You swallow the tablet, and stomach acid dissolves the iron salt into free iron ions.
2. The iron moves into your duodenum (the first part of your small intestine), where special transporter proteins on the gut cells pull it inside.
3. The iron crosses into your bloodstream and binds to transferrin (a carrier protein that shuttles iron safely through the blood).

4. Transferrin delivers the iron to your bone marrow, where young red blood cells grab it and use it to build hemoglobin.
5. With enough iron on hand, your marrow cranks out healthy, full-sized red cells that can carry normal amounts of oxygen.

SAFETY WATCH

Constipation and dark or black stools are very common and harmless (the iron stains your stool). · Nausea, stomach cramps, and upset stomach happen in about one in five people; taking the pill every other day with food cuts this risk in half. · Do NOT take iron at the same time as calcium supplements, antacids, or tea—they all block absorption. Space them at least two hours apart. · Vitamin C (orange juice, a small glass) taken with your iron tablet boosts absorption. · Keep iron tablets locked away from small children—accidental overdose in toddlers can cause severe poisoning, including liver damage and shock.

Intravenous iron (ferric carboxymaltose, iron sucrose, iron dextran, ferumoxytol) · Intravenous iron supplement

IV iron delivers a large dose of iron straight into your bloodstream, skipping your gut entirely. This is the go-to choice when your intestine can't absorb oral iron well (celiac disease, Crohn's, gastric bypass), when oral iron makes you too sick to take it, when you need your iron stores refilled fast (severe anemia, upcoming surgery, third trimester of pregnancy), or when you are on dialysis for kidney failure (dialysis pulls iron out, and the kidneys stop making erythropoietin, the hormone that tells your marrow to make red cells).

1. The iron is bound in a stable complex (a sugar shell) that keeps it from causing irritation or clumping in the vein.
2. The infusion runs over 15 to 60 minutes (depending on the formulation), and the iron-complex molecules circulate in your blood.
3. Macrophages (clean-up immune cells) in your liver and spleen capture the complexes and gently pull the iron free.
4. The freed iron binds to transferrin and is carried to your bone marrow.
5. Your marrow uses the iron to build hemoglobin, and healthy red cells start rolling off the assembly line within days.

SAFETY WATCH

Allergic or hypersensitivity reactions (flushing, itching, chest tightness, low blood pressure) are rare (less than 1 in 200) but can happen during or right after the infusion; the nurse watches you closely and has rescue medicines ready. · Iron dextran (the oldest formulation) carries a slightly higher reaction risk, so many centers now prefer ferric carboxymaltose, iron sucrose, or ferumoxytol. · A harmless side effect: your blood iron and ferritin levels will jump very high right after the infusion, so recheck labs at least two to four weeks later to see the true steady-state. · Do NOT give IV iron during an active infection or if you have iron overload (hemochromatosis)—extra iron can feed bacteria and damage organs. · Rarely, free iron can stain skin at the IV site (leave a faint brown mark); using good IV technique prevents this.

Red flags

- Blood in your stool (black, tarry stools or bright red blood) or vomiting blood — can mean bleeding in your stomach or intestines
- Sudden, severe chest pain or trouble breathing — your heart may be struggling because of very low oxygen
- Ongoing heavy menstrual bleeding that soaks through a pad or tampon every hour — can lead to dangerous iron loss
- Unintended weight loss, belly pain, or trouble swallowing — could signal a hidden source of bleeding like cancer or an ulcer
- Signs of severe anemia: confusion, fainting, extreme weakness, or very fast heartbeat at rest — means your organs aren't getting enough oxygen

Nursing priorities

1. Check hemoglobin, blood pressure, and heart rate before and after position changes to assess severity and hemodynamic stability — Hemoglobin below 7 g/dL or orthostatic low blood pressure (hypotension) (drop in blood pressure when standing) means tissues are not getting enough oxygen and may require urgent transfusion before waiting for iron to work
2. Verify ferritin, serum iron, TIBC, and transferrin saturation labs are drawn before giving any iron supplementation — Iron therapy falsely raises these lab values within 24 hours, preventing accurate diagnosis of the type of anemia and potentially masking coexisting conditions like anemia of chronic disease

3. Educate patient to take oral iron (ferrous sulfate 325 mg) every other day on an empty stomach, one hour before breakfast — Every-other-day dosing allows hepcidin (a hormone blocking iron absorption) to drop between doses, improving absorption by 30 percent and reducing constipation and nausea compared to daily dosing
4. Teach patient to take iron with vitamin C (orange juice or 250 mg tablet) and avoid calcium, antacids, or tea within two hours — Ascorbic acid (vitamin C) keeps iron in the ferrous form for better absorption in the acidic duodenum, while calcium and tannins in tea bind iron into non-absorbable complexes
5. Warn patient their stools will turn black and not to stop iron therapy thinking they have bleeding — Black stools from oral iron (non-tarry, no foul odor) are harmless unabsorbed iron pigment, different from black tarry stool (melena) which is shiny, sticky, and smells like digested blood from GI bleeding (hemorrhage)
6. Schedule follow-up hemoglobin check in four weeks and monitor for reticulocyte rise in seven to ten days as first sign of response — Reticulocytes (young red blood cells) increase first when bone marrow responds to iron; hemoglobin rises by 1 g/dL per week if treatment is working, but ferritin stores take three to six months to replenish
7. Coordinate colonoscopy referral for men and postmenopausal women with new iron deficiency even without GI symptoms — Occult colon cancer or advanced adenomas bleed slowly without visible blood or pain; iron deficiency may be the only early warning sign in older adults
8. Arrange IV iron infusion (ferric carboxymaltose 750 mg) if patient has inflammatory bowel disease, chronic kidney disease, or cannot tolerate oral iron after two weeks — Inflammation raises hepcidin which blocks intestinal iron absorption and traps iron in macrophages; IV iron bypasses the gut and directly replenishes stores when oral therapy fails

Sources

- American Gastroenterological Association (AGA) Clinical Practice Update on Evaluation and Management of Iron Deficiency Anemia, 2020
- CDC guideline on Iron and Iron Deficiency
- American Society of Hematology (ASH) clinical guidelines
- World Health Organization (WHO) guideline on iron supplementation

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