

# Vitamin B12 Deficiency & Pernicious Anemia

Vitamin B12 deficiency happens when your body does not absorb enough B12 from food, often because the stomach stops making a special protein called intrinsic factor. Pernicious anemia is the most common type, caused by an autoimmune attack on stomach cells that make intrinsic factor.

## THE ONE-LINE TRUTH

Without intrinsic factor or adequate B12 absorption, the body cannot make healthy red blood cells or maintain nerve sheaths, leading to macrocytic anemia and irreversible neurologic damage if untreated.

## The chain — how it unfolds

1. Intrinsic factor production stops or B12 intake is inadequate — why: Autoimmune destruction of parietal cells, ileal disease, or dietary deficiency blocks B12 absorption
2. Serum B12 levels drop below 200 pg/mL and tissue stores deplete over months to years — why: The liver's stored B12 runs out, and daily losses through bile and urine are not replaced
3. DNA synthesis slows in rapidly dividing cells (bone marrow, intestinal lining) — why: B12 is essential for converting folate to its active form (methyltetrahydrofolate) needed to build DNA bases
4. Megaloblastic anemia develops with macrocytic red cells and low reticulocyte count — why: Red blood cell precursors grow large but cannot divide, leading to ineffective erythropoiesis and low counts of all blood cells (pancytopenia) (low counts of all blood cells)
5. Homocysteine and methylmalonic acid (MMA) accumulate in blood and tissues — why: B12 deficiency blocks the enzymes (methionine synthase and methylmalonyl-CoA mutase) that break down these toxic metabolites
6. Myelin sheath degenerates in spinal cord and peripheral nerves (subacute combined degeneration) — why: High MMA levels damage mitochondria in nerve cells, and impaired methionine synthesis prevents myelin repair

7. Progressive neurologic symptoms appear: tingling or numbness (paresthesias), loss of coordination (ataxia), loss of proprioception, dementia — why: Posterior and lateral spinal columns degenerate (combined systems disease), and peripheral nerve axons die, causing irreversible damage if untreated beyond 6-12 months
8. Severe anemia causes high-output heart failure, and untreated neurologic damage becomes permanent — why: The heart cannot sustain increased workload to compensate for severe anemia, and dead nerve axons do not regenerate even with B12 replacement

## Spot it — what you see, and why

---

- Fatigue and weakness: Without B12, red blood cells become large and fragile (macrocytes), carry less oxygen, and deliver less energy to muscles and tissues
- Pale or yellowish skin (jaundice): Fragile oversized red blood cells break apart easily in the bloodstream (hemolysis), releasing bilirubin that turns skin yellow
- Numbness or tingling in hands and feet (paresthesias): B12 is required to build the fatty myelin sheath that protects nerves; without it, nerve signals travel poorly, especially in the longest nerves
- Difficulty walking or balance problems: Damage to the posterior columns of the spinal cord (subacute combined degeneration) disrupts position sense and coordination
- Sore, red tongue (glossitis): Rapidly dividing cells in the tongue lining need B12 to make DNA; without it, they cannot replace themselves and the tongue becomes smooth and inflamed
- Memory problems or confusion: Brain neurons depend on myelin for fast signaling and on B12-dependent enzymes to clear toxic homocysteine and methylmalonic acid that damage brain tissue

## Red flags — act now

---

- New numbness, tingling, or weakness in legs with difficulty walking (subacute combined degeneration requires urgent B12 replacement to prevent permanent disability)
- Confusion, memory loss, or personality change in a patient with macrocytic anemia (neuropsychiatric manifestations of B12 deficiency)
- Severe anemia (hemoglobin below 7 g/dL) with chest pain, shortness of breath, or altered mental status (risk of high-output heart failure; may need transfusion)
- Low counts of all blood cells (Pancytopenia) (low red cells, white cells, and platelets) with macrocytosis (can mimic acute leukemia or myelodysplastic syndrome; needs urgent hematology evaluation)

## Treat it — in this order

---

1. Cyanocobalamin or hydroxocobalamin intramuscular injection → Bypasses the gut entirely, delivering B12 directly into muscle where it is absorbed into the bloodstream; corrects anemia within 6–8 weeks and begins reversing nerve damage within days if caught early
2. High-dose oral cyanocobalamin (1000–2000 mcg daily) → Even without intrinsic factor, about 1% of a large oral dose is absorbed by passive diffusion across the intestinal lining; this can maintain B12 levels after initial correction with injections
3. Sublingual or nasal B12 formulations → Absorbed through mucous membranes in the mouth or nose, avoiding the need for injections and bypassing gut absorption problems; useful for patients who refuse injections or have needle phobia
4. Red blood cell transfusion → Immediately increases oxygen-carrying capacity in patients with severe symptomatic anemia (hemoglobin below 7 g/dL with chest pain, shortness of breath, or altered mental status); stabilizes the patient while B12 replacement takes effect
5. Folate supplementation (with B12 replacement, never alone) → Corrects the anemia by allowing DNA synthesis to proceed; both B12 and folate are needed as cofactors in the methylation cycle and nucleotide production

## Your top priorities at the bedside

---

1. Monitor for signs of worsening neurologic damage (numbness, tingling, balance problems, memory loss) — why: Vitamin B12 deficiency causes demyelination (loss of protective nerve covering) in the spinal cord and peripheral nerves. Early detection and treatment can reverse symptoms, but delays may cause permanent nerve damage.
2. Assess for fall risk related to peripheral neuropathy and gait instability — why: B12 deficiency damages the posterior columns (nerve pathways in the spinal cord that control position sense), leading to loss of coordination (ataxia) (unsteady walking) and increased fall risk, especially in older adults.
3. Educate about lifelong B12 replacement therapy for pernicious anemia — why: Pernicious anemia results from autoimmune destruction of parietal cells (stomach cells that make intrinsic factor needed to absorb B12). Patients cannot absorb oral B12 and require injections or high-dose oral therapy forever.