

Vitamin B12 Deficiency & Pernicious Anemia

A plain-English guide for you and your family

WHAT IS HAPPENING

Normally, your stomach makes a special helper protein called intrinsic factor that grabs onto vitamin B12 from the food you eat and carries it into your bloodstream through the small intestine. Your body uses B12 to build healthy red blood cells and to keep the protective coating on your nerves working well. In pernicious anemia, your immune system mistakenly attacks the stomach cells that make intrinsic factor, so B12 cannot get absorbed even if you eat plenty of it. Without enough B12, your red blood cells grow too large and do not work right, and the coating on your nerves starts to break down, causing numbness, tingling, and balance problems. This condition develops slowly over months to years, and early treatment with B12 injections or high-dose pills can reverse most symptoms and prevent permanent nerve damage.

What you might feel

- Fatigue and weakness
- Pale or yellowish skin (jaundice)
- Numbness or tingling in hands and feet (paresthesias)
- Difficulty walking or balance problems
- Sore, red tongue (glossitis)
- Memory problems or confusion
- Shortness of breath
- Rapid or irregular heartbeat (palpitations)

Call the doctor right away if...

- 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)

What the care team will do

- Monitor for signs of worsening neurologic damage (numbness, tingling, balance problems, memory loss)
- Assess for fall risk related to peripheral neuropathy and gait instability
- Educate about lifelong B12 replacement therapy for pernicious anemia
- Monitor complete blood count and reticulocyte response after treatment initiation
- Screen for other autoimmune conditions (thyroid disease, type 1 diabetes, vitiligo)
- Assess dietary intake in patients with vegan or vegetarian diets
- Monitor potassium levels closely during initial B12 replacement therapy
- Evaluate for reversible causes including medications (metformin, proton-pump inhibitors) and gastric surgery

Medicines you may be given — and why

Cyanocobalamin intramuscular

This synthetic form of vitamin B12 is injected into muscle and absorbed into the bloodstream. Inside cells, enzymes remove the cyanide part and convert cyanocobalamin into the two active forms the body uses: methylcobalamin (for the methylation cycle) and adenosylcobalamin (for energy production in mitochondria). These active forms serve as helper molecules (cofactors) for two essential enzymes: methionine synthase (which recycles folate and makes DNA building blocks) and methylmalonyl-CoA mutase (which breaks down certain fats and proteins for energy).

Hydroxocobalamin intramuscular

Hydroxocobalamin is another synthetic form of B12, similar to cyanocobalamin but with a hydroxyl (OH) group instead of cyanide. It is injected into muscle and absorbed into the bloodstream, where it binds more tightly to transport proteins and stays in the body longer than cyanocobalamin. Cells convert it to the two active forms (methylcobalamin and adenosylcobalamin) in the same way. The longer retention time may allow for less frequent dosing, and it is preferred in patients with cyanide toxicity or tobacco amblyopia (a rare type of vision loss from cyanide in tobacco smoke).

Cyanocobalamin oral high-dose

Even without intrinsic factor, about 1–2% of an oral B12 dose is absorbed by passive diffusion directly through the cells lining the small intestine. When the dose is very high (1000–2000 mcg), this small percentage provides enough B12 to meet daily needs (2–3 mcg per day). After absorption, the vitamin enters the bloodstream, binds to transport proteins, and is delivered to tissues where it is converted to active forms. This approach works for maintenance after initial correction with injections, or as primary treatment in patients with mild deficiency and no neurologic symptoms.

Folic acid (folate) oral

Folic acid is a synthetic form of folate, a B-vitamin that works closely with B12 in the methylation cycle. After absorption in the small intestine, folic acid is converted to tetrahydrofolate (THF) and then to 5-methyltetrahydrofolate (5-methyl-THF), the active form. Methionine synthase (the B12-dependent enzyme) transfers the methyl group from 5-methyl-THF to homocysteine, making methionine and regenerating THF. THF is then used to build purines and thymidine, the building blocks of DNA, so cells can divide. Folate supplementation corrects the anemia in B12 deficiency by allowing DNA synthesis, but it does not prevent or treat nerve damage because it does not supply the adenosylcobalamin needed for myelin synthesis and mitochondrial function.

Packed red blood cells (transfusion)

Packed red blood cells (PRBCs) are donated red blood cells separated from plasma and white cells, then stored in a preservative solution. When transfused into a vein, these cells immediately increase the oxygen-carrying capacity of the blood. Each unit raises the hemoglobin by about 1 g/dL in an average adult. In severe B12-deficiency anemia with symptoms (chest pain, severe shortness of breath, altered mental status, hemoglobin below 7 g/dL), transfusion provides life-saving oxygen delivery while B12 replacement takes days to weeks to stimulate new red blood cell production. Transfused cells have a normal lifespan (about 120 days), but the underlying deficiency will cause anemia to recur unless B12 is replaced.

Dietary modification (animal-product inclusion or fortified foods)

Vitamin B12 is naturally found only in animal products: meat, fish, poultry, eggs, and dairy. Some foods (breakfast cereals, plant-based milks, nutritional yeast) are fortified with synthetic B12. In people who can absorb B12 normally (intact stomach and terminal ileum, adequate intrinsic factor), eating these foods provides the 2–3 mcg of B12 needed daily. The stomach releases B12 from food proteins using acid and pepsin, then intrinsic factor binds the free B12 and carries it to the ileum for absorption. Dietary modification alone cannot treat established

deficiency or pernicious anemia, but it can prevent deficiency in vegans and maintain B12 status after medical treatment corrects a deficiency.

Where this information comes from

- American Society of Hematology (ASH) guidelines on the evaluation and management of vitamin B12 deficiency (2020)
- National Institute for Health and Care Excellence (NICE) clinical guideline on vitamin B12 deficiency and pernicious anemia diagnosis and treatment (2019)
- UpToDate clinical overview: 'Causes and pathophysiology of vitamin B12 and folate deficiency' and 'Treatment of vitamin B12 and folate deficiencies' (2023)
- Centers for Disease Control and Prevention (CDC) recommendations for vegetarian and vegan nutrition including B12 supplementation guidance (2022)

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