Folate Deficiency Anemia

A plain-English guide for you and your family

WHAT IS HAPPENING

Normally, your bone marrow makes millions of fresh red blood cells every day using folate as a key building block for DNA. When folate runs low—from not eating enough greens and fortified grains, from drinking too much alcohol, or from certain medicines—the marrow cannot finish building cells correctly. The new red blood cells grow too large and their DNA is fragile, so they die early or never leave the marrow. Over weeks to months, you feel tired, look pale, and may notice a sore tongue or tingling in your hands and feet because oxygen is not reaching your tissues well.

What you might feel

- Extreme tiredness that does not improve with rest
- Pale or yellowish skin and eyes
- Shortness of breath during usual activities
- Sore red tongue (glossitis)
- Rapid heartbeat or chest pain
- Tingling or numbness in hands and feet
- Diarrhea and poor appetite
- Confusion or difficulty concentrating

Call the doctor right away if...

- New confusion, difficulty walking, or loss of balance (may indicate B12 deficiency with spinal cord damage, not just folate deficiency)
- Chest pain or shortness of breath at rest (signals severe anemia causing heart strain or heart failure)
- Pregnancy with folate deficiency (high risk of neural tube defects in the developing fetus)
- Hemoglobin below 7 g/dL or signs of shock (pale, sweaty, rapid pulse, low blood pressure)

What the care team will do

- Assess neurological status for signs of folate-related nerve damage
- Monitor for signs of tissue low oxygen (hypoxia) from severe anemia
- Identify and address dietary causes of folate deficiency
- Screen pregnant or reproductive-age women immediately
- Review medications that interfere with folate metabolism
- Differentiate folate deficiency from vitamin B12 deficiency before treatment
- Educate on proper folic acid supplementation and expected response time
- Assess for underlying malabsorption disorders if dietary intake is adequate

Medicines you may be given — and why

folic acid

Folic acid is a synthetic form of folate that the body converts into tetrahydrofolate (the active form). Tetrahydrofolate carries one-carbon units needed to build purines and thymidine, which are the building blocks of DNA. Without adequate folate, cells cannot divide properly, especially rapidly dividing cells like red blood cell precursors in the bone marrow.

cyanocobalamin (vitamin B12)

Cyanocobalamin is a form of vitamin B12 that the body converts into methylcobalamin and adenosylcobalamin, the active forms. These cofactors work with folate in DNA synthesis and are also essential for myelin (nerve coating) formation. B12 must be given along with folate if both deficiencies exist, because treating folate alone will not protect the nerves.

leucovorin (folinic acid)

Leucovorin is already in the tetrahydrofolate form, so it does not require conversion by dihydrofolate reductase. It is used to rescue normal cells during high-dose methotrexate chemotherapy, because methotrexate blocks dihydrofolate reductase and stops all folate activity. Leucovorin bypasses the blocked enzyme and allows healthy cells to make DNA while the cancer cells remain suppressed.

Dietary modification (folate-rich foods)

Folate occurs naturally in foods as polyglutamate folate, which is converted to monoglutamate folate in the intestine before absorption. Green leafy vegetables (spinach, kale), legumes (lentils, black beans), and fortified grains provide high folate content. The United States mandates folic acid fortification of enriched grain products, which has significantly reduced folate deficiency and neural tube defects.

Packed red blood cell transfusion

Transfusion delivers donor red blood cells that immediately carry oxygen to tissues. It is reserved for patients with dangerously low hemoglobin (usually below 7 g/dL) or those with symptoms of heart failure or severe low oxygen (hypoxia) (low oxygen). Transfusion is a bridge therapy while folate supplementation takes time to stimulate the bone marrow to produce new cells.

Where this information comes from

- American Society of Hematology (ASH) guidelines on the evaluation and management of macrocytic anemia and megaloblastic disorders (2021)
- Centers for Disease Control and Prevention (CDC) recommendations for folic acid supplementation for prevention of neural tube defects (2020)
- National Institutes of Health (NIH) Office of Dietary Supplements fact sheet on folate for health professionals (2022)
- American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin on neural tube defects and periconceptional folic acid supplementation (2017, reaffirmed 2021)

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