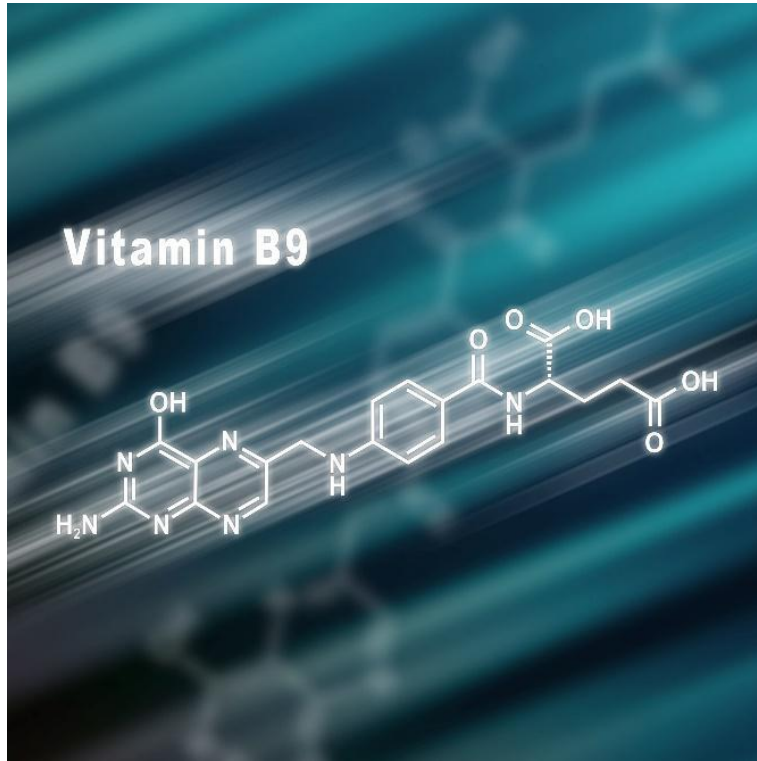


# Folic Acid



by Stefanie Schwartz, MS, RD, CDN and Rich Strongwater, MD

Folic acid is a water-soluble B vitamin (vitamin B-9) that plays a key role in cell growth and DNA and RNA synthesis. Folate is the naturally occurring form in food, whereas folic acid is the synthetic version present in fortified foods. In over 80 countries (and in many countries, government mandated), wheat and corn flour is routinely fortified with folic acid.

Folate is the measured form in blood, with a normal serum folate level exceeding 6.5 ng/mL. Tetrahydrofolate is the more potent form of synthetic supplementation. Note that folate deficiency may take 8-16 weeks to develop if your diet becomes deficient in folic acid.

Adequate folic acid levels is essential for:

- Purine and pyrimidine synthesis (the building blocks of DNA and RNA)
- Nucleoprotein synthesis (important in essential biological functions)
- Maintaining erythropoiesis (production of red blood cells)

The National Institutes of Health recommend that all adults  $\geq 19$  years of age consume at least 400 mcg/day (through supplementation or from food), although 1,000 mcg/day from supplementation is the upper limit. During childbearing years, to help prevent neural-tube defects, women should take 600 mcg/day of folic acid, by supplementation, starting 1 month

before conception through 12 weeks of pregnancy. Generally, most women continue 400 to 800 micrograms of folic acid supplementation during pregnancy.

Folic acid also lowers homocysteine levels; however, this has not been directly correlated with reducing heart disease. High homocysteine levels appears to be a marker for arteriosclerosis. One downside to folic acid supplementation is that too much folic acid intake may be associated with a higher risk of certain malignancies.

## **Signs and Symptoms of Folate Deficiency**

Folic-acid deficiency can cause fatigue, weakness, shortness of breath, mouth sores, confusion, depression, and megaloblastic anemia. Severe folate deficiency can cause severe neurologic complications. Another sign of folic acid deficiency is an enlarged and painful red tongue.

## **Causes and Risk Factors of Folate Deficiency**

Risk factors for folate deficiency include alcoholism, malnutrition, scurvy, liver disease, hemodialysis, celiac disease, sideroblastic anemia, pregnancy, Whipple disease, and amyloidosis.

Other risk factors for folate deficiency include:

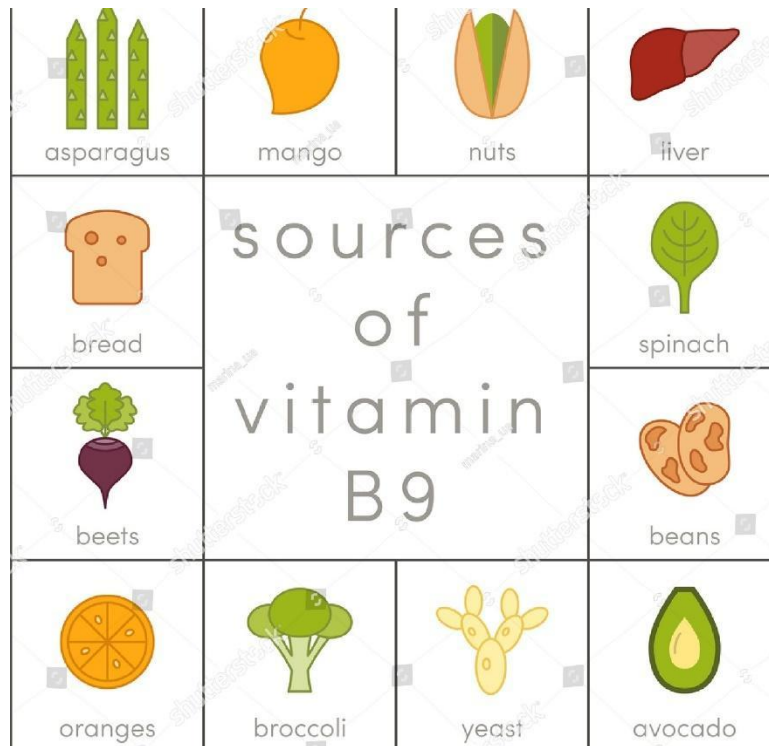
- Taking medications such as methotrexate, phenytoin, sulfasalazine, and trimethoprim
- Low socioeconomic status and/or institutionalization leading to inadequate intake of green leafy vegetables or malnutrition in general
- Other illnesses affecting the jejunum (where folate is absorbed) include celiac disease, tropical sprue, short bowel syndrome, amyloidosis, gastric bypass, and mesenteric vascular insufficiency

## **Caution with Supplementation**

Administer folic-acid supplements with care, as they may interfere with several medications, including fosphenytoin sodium injection (Cerebyx), methotrexate, phenobarbital (Luminal), phenytoin (Dilantin), primidone (Mysoline), and pyrimethamine (Daraprim). When taking methotrexate on a weekly basis, do not take folic acid the same day as the methotrexate. When supplementing with folic acid while on antiepileptic medications, careful monitoring of the antiepileptic medication levels is warranted.

## **Pearl to Know**

Foods high in folate include fortified cereals, green leafy vegetables, asparagus, broccoli, lentils, black-eyed peas, Brussel sprouts, papaya, oranges, and sunflower seeds.



## References:

Williamson MA, Snyder LM. Folate, serum and erythrocytes. *Wallach's Interpretation of Diagnostic Tests (Interpretation of Diagnostic Tests)*. 9th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2011:180-181.

Kashif M. Khan; Ishwarlal Jialal. Folic Acid Deficiency. StatPearls Publishing LLC. NIH. National Library of Medicine. Last Update: May 8, 2022. Bookshelf ID: NBK535377 PMID: [30570998](https://pubmed.ncbi.nlm.nih.gov/30570998/)

Tablante EC, Pachon H, Guetterman , Finkelstein J. Fortification of wheat and maize flour with folic acid for population health outcomes. Cochrane Database of Systematic Reviews. July 2019. <https://doi.org/10.1002/14651858.CD012150.pub2>

Nayyar AS, Nataraju B, Subhas GT. Phenytoin-Folate Interactions: How Far is Safe Folate Supplementation in Phenytoin Treated Epileptic Patients? Journal of Applied Pharmaceutical Science 02 (06); 2012: 230-235.

Murphy M, Westmark C. Folic Acid Fortification and Neural Tube Defect Risk: Analysis of the Food Fortification Initiative Dataset. Nutrients. 2020 Jan; 12(1): 247.  
Published online 2020 Jan 18. doi: [10.3390/nu12010247](https://doi.org/10.3390/nu12010247)