

Why You Should Only Take Folate and Never Folic Acid

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STORY AT-A-GLANCE

- > It's extremely rare to get too much folate from foods, but it is possible to get too much folic acid, the synthetic version of folate found in supplements and fortified foods
- > In pregnant mice, high levels of folic acid harmed brain development in offspring, and low levels of vitamin B12 made the damage worse
- > The combination of low vitamin B12, which often occurs in people eating vegan or vegetarian diets, along with high folic acid, could be increasing neurodevelopment disorders in children
- > Due to prenatal supplements and fortified foods, many people have abnormally high levels of folic acid
- Studies looking into the effects of folic acid on autism development are conflicting, with some showing a protective effect, but a growing body of evidence points to potential harms when consumed in excess

The terms folate and folic acid are often used interchangeably, but they're not the same. Folic acid is the synthetic version of folate, or vitamin B9. While folate is found naturally in foods like leafy greens, folic acid is found in supplement form as well as in fortified foods, such as cereal and bread.

It's extremely rare to get too much folate from foods, but it is possible to get too much folic acid,¹ with potentially significant adverse effects. In pregnant mice, high levels of

folic acid harmed brain development in offspring, and low levels of vitamin B12 made the damage worse.

The combination of low vitamin B12, which often occurs in people eating vegan or vegetarian diets, along with high folic acid "could potentially be driving neurodevelopment problems among children in the U.S.," independent journalist Nina Teicholz tweeted.²

Folic Acid Food Fortification May Have a Dark Side

In the 1990s, U.S. health officials recommended that women who may become pregnant should take 400 micrograms (mcg) of folic acid daily to reduce the risk of having a baby with neural tube defects. However, since the neural tube closes early on during pregnancy — about 28 days after conception — some women may miss the vulnerable period during which folate is critical.

"For folate to be effective, it must be taken in the first few weeks after conception, often before a woman knows she is pregnant," explains the Harvard School of Public Health.³ This is why the U.S. Food and Drug Administration started folic acid fortification in foods in 1998.⁴ It's now required that folic acid be added to enriched breads, flour, cornmeal, pastas, rice and other foods made with cereal grains.⁵

According to the CDC, neural tube defects have decreased since the beginning of folic acid fortification, such that "about 1,300 babies are born each year without a neural tube defect who might otherwise have had a neural tube defect."⁶ But while neural tube defects have declined, other health conditions — namely neurodevelopmental disorders — have risen.

"There's no doubt the introduction of folic acid diet fortification has been beneficial, substantially lowering the incidence of neural tube defects," Ralph Green, UC Davis professor in the Department of Pathology and Laboratory Medicine, said in a news release. "However, too much folic acid may have detrimental impacts on brain development, and that's something we need to sort out."⁷ Davis and colleagues conducted a study that found excess folic acid is associated with neurodevelopmental risks, especially in concert with vitamin B12 deficiency⁸ – a significant concern as folic acid intake has grown.

Many People Have Abnormally High Levels of Folic Acid

"The food industry has been adding folic acid to breakfast cereals, snack foods, and vitamins, and that has likely increased intake above recommended guidelines," Green said. "The safe upper limit for folate is 1,000 micrograms per day. The National Health and Nutrition Examination Survey data showed that a substantial percentage of women's diets were above that limit."⁹

Many women consume folic acid not only in fortified foods but also in prenatal vitamins. The study, published in Communications Biology, noted, "[T]otal folate intake, largely in the form of FA [folic acid], has risen substantially as have blood folate levels in populations, with a considerable proportion persistently exhibiting extreme supraphysiological concentrations in their blood, as well as increases in unmetabolized folic acid (UMFA) in those taking supplements."¹⁰

Meanwhile, both too little and too much folic acid during pregnancy may influence neurodevelopment in offspring, previous research has found, by modulating prenatal neurogenesis.¹¹ High amounts of supplemental folic acid - 1,000 µg per day or more during pregnancy have also been linked with impairments in neurocognitive development in 4- to 5-year-old children.¹²

Other research revealed that daily folic acid doses of more than 5,000 μ g led to reduced psychomotor development in children compared to children whose mothers took lower doses of 400 to 1,000 μ g.^{13,14}

Neurodevelopmental Disorders Skyrocketed Since Folic Acid Fortification

As folic acid in foods increased, so, too, have neurodevelopmental disorders. "Data collected by the Centers for Disease Control and Prevention suggest that in recent decades several neurodevelopmental disorders have seen considerable rises in prevalence, chief amongst them autism spectrum disorder (ASD), but also attention deficit hyperactivity disorder (ADHD) and epilepsy," according to the Communications Biology study.¹⁵

CDC data show that 1 in 36 U.S. children has autism¹⁶ – up from 1 in 10,000 in the 1970s.¹⁷ The rapid rise suggests environmental factors are involved. "One environmental exposure that has increased substantially over recent decades is intake of the B vitamin folate in the synthesized, oxidized form of folic acid," the researchers wrote.¹⁸

While studies looking into the effects of folic acid on autism development are conflicting, with some showing a protective effect, a growing body of evidence points to potential harms when consumed in excess. The scientists explained:¹⁹

"Some of the latest research in this area using data from the Boston Birth Cohort uncovered a positive association between maternal plasma folate levels and autism risk. Autism incidence was greatest in children born to mothers with the highest maternal plasma folate levels, exceeding the cutoff suggested by the WHO (>45.3 nmol/L).

Moreover, subsequent work showed that children with cord blood levels of unmetabolized FA (UMFA) in the highest, versus lowest quartile, had a greater risk for developing ASD.

Similarly, a Swedish study testing association of 62 maternal blood biomarkers during early pregnancy with later ASD diagnosis identified total folate as having the highest odds ratio at 1.7. These results are supported by epidemiological investigations from the Rochester Epidemiological Project in Rochester, MN and earlier CDC data."

Even Moderately High Folic Acid May Harm Brain Development

For the study, researchers investigated folic acid intake in mice on brain development in their offspring, specifically the cerebral cortex, which plays a role in cognitive and emotional functions, as well as psychiatric disorders. One group of mice was fed normal levels of folic acid and B12, while four other groups were fed diets including:²⁰

- High folic acid
- Low vitamin B12
- High folic acid and low vitamin B12
- High folinic acid, a natural folate

While the natural folate led to no changes to the developing mouse brains, changes in neural development occurred with exposure to high levels of folic acid. The most pronounced abnormalities occurred in those given high folic acid low vitamin B12. Study author Konstantinos Zarbalis, professor of pathology and laboratory medicine, explained:²¹

"These different dietary conditions appear to influence the way neurons arise in the developing brain. With high levels of folic acid or B12 deficiency, there was a change in neural development.

Cortical neurons that usually emerge during a later stage of brain development were produced over a longer period of time and required a longer period to settle in and assume their proper position in the developing brain. In addition, both high folic acid and B12 deficiency appear to cause many neurons to develop fewer interconnections."

The team found that "even moderately excessive amounts" of folic acid had a detrimental effect on prenatal cortical development, which was made worse by vitamin B12 deficiency.²²

The Folate Cycle Depends on Vitamin B12

The findings highlight the complex interplay that occurs between various nutrients in your body, and why proper balance is so critical to optimal health. This is particularly true for folic acid and vitamin B12. According to the Communications Biology study:²³

"The folate cycle is critically dependent on the availability of the essential micronutrient, vitamin B12 (B12), which is a required cofactor for the methionine synthase reaction in which homocysteine is converted to methionine through transfer of a methyl group from N-5-methyltetrahydrofolate (CH3-THF). B12 is needed for this reaction to enable folate cycle progression and regeneration of tetrahydrofolate (THF) from CH3-THF.

In the absence of B12, folate becomes functionally trapped in the form of CH3-THF. This suggests that the effects of FA excess, which paradoxically may decrease functional folate availability, can be further exacerbated by B12 deficiency, as studies on cognitive performance of older adults have suggested."

Vitamin B12, also known as cobalamin, is necessary for your body to make red blood cells as well as for proper nerve function and DNA synthesis. Without adequate levels, a number of physical symptoms, ranging from numbness to fatigue, can occur. Mental health can also suffer significantly, as vitamin B12 plays an important role in neurological function.

It's been shown, for instance, that people with depression and high B12 levels have better responses to treatment,²⁴ while up to 30% of patients hospitalized for depression may be B12 deficient.²⁵

The only reliable and absorbable sources of vitamin B12 are animal products, which is why vegans or strict vegetarians who abstain from animal products and do not supplement their diet with vitamin B12 will often become deficient and may face increased risks of neuropsychiatric and neurological problems as a result.²⁶

As Teicholz tweeted, "In many countries, pregnant women for decades have been told to take folic acid to prevent neural tube defects in their babies. Yet folic acid also added to refined grains (which we eat a LOT of) ... sending folic acid levels [up]. Low B12 occurs

with vegan/vegetarian diets," which could be responsible for increasing neurodevelopmental disorders among U.S. children.²⁷

Where to Find Natural Folate

While too much synthetic folic acid in fortified processed foods and supplements may be problematic, your body needs natural folate in your diet for optimal mitochondrial function,²⁸ protein metabolism and breaking down homocysteine, which can be harmful in high amounts.²⁹

The best way to increase your levels of this important micronutrient is to eat foods rich in natural folate, which include asparagus, avocados, Brussels sprouts, broccoli and spinach. Meanwhile, vitamin B12-rich foods include grass fed beef liver, wild rainbow trout and wild sockeye salmon. If you suspect you may be deficient, weekly B12 shots or a high-dose, daily supplement may be necessary.

Sources and References

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