ISPN
INTERNATIONAL SOCIETY FOR PEDIATRIC NEUROSURGERY

ISPN Statement on the Safety of Folic Acid Fortification Focused on Cancer and other Health Risks

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Statement of purpose

The International Society for Pediatric Neurosurgery (ISPN) recognizes the critical importance of folic acid fortification as a public health intervention to prevent neural tube defects (NTDs), one of the most severe and preventable forms of congenital disability affecting the central nervous system. The global pediatric neurosurgical community, including ISPN members who routinely care for children with spina bifida and related conditions, has witnessed firsthand the lifelong impact of NTDs on patients, families, and health systems.

In light of recent concerns expressed in India and other countries regarding the possible association between folic acid fortification and increased cancer risk, the ISPN wishes to reaffirm the overwhelming scientific consensus on the **safety and efficacy** of folic acid when used at recommended levels for food fortification.

Recommended Levels and Safety Profile

The World Health Organization (WHO) recommends adding **0.5 to 1.5 milligrams of folic acid per kilogram of flour or fortified food**, a concentration shown to be safe and effective for reducing NTD incidence. This range is not associated with toxicity or adverse health effects. Folic acid is a water-soluble vitamin; excess amounts are excreted through urine.

Concerns regarding the presence of unmetabolized folic acid in the bloodstream have not been linked to any demonstrated harm. Reputable health authorities, including the WHO, the U.S. Centers for Disease Control and Prevention (CDC), and public health agencies in over 80 countries with mandatory fortification programs, have consistently concluded that **folic acid fortification at the WHO-recommended levels is safe.**

Evidence on Cancer Risk

The question of a potential link between folic acid and cancer, particularly colorectal cancer, has been extensively studied. Two different comprehensive meta-analysis of **randomized controlled trials involving more than 50,000 participants** found no increased or decreased risk of cancer—including colorectal, breast, lung, or prostate cancer - among those consuming folic acid.

While one 2007 study reported an increased rate of colorectal adenomas in a specific high- risk group receiving 1,000 mcg daily over several years, this finding has not been replicated in subsequent large-scale trials. In contrast, most evidence indicates **no causal link** between folic acid intake and cancer incidence, and some studies have even noted a **potential protective effect** of dietary folate against certain cancers, such as pancreatic and breast cancer.

Other Health Concerns

Beyond cancer, several other potential risks have been considered, yet none have been supported by conclusive evidence at the levels used in food fortification:

- **Vitamin B12 Deficiency**: Folic acid was previously thought to potentially "mask" B12 deficiency, especially in older adults. However, with modern diagnostic tools and routine lab testing, B12 deficiency can be accurately identified, and fortification does not delay diagnosis or treatment.

- **Cognitive Issues and Autism**: While some observational studies have explored associations between folic acid and neurodevelopmental outcomes such as autism or cognitive function, no causal relationship has been demonstrated, and evidence remains inconclusive.

- **Asthma and Allergies**: A few early studies raised concerns about possible links to childhood asthma, but more recent and robust research has not confirmed any such effect.

- **Twin Pregnancies**: Some reports suggested a higher incidence of twin births with periconceptional folic acid supplementation. However, this association is weak, and it does not outweigh the significant public health benefits of preventing NTDs.

- **Malaria**: Some concerns have arisen in the context of high-dose iron and folic acid supplements in malaria-endemic areas. However, the much lower doses used in food fortification have not been linked to any increase in malaria risk.

Other Proven and Potential Health Benefits of Folic Acid Fortification

Beyond the prevention of neural tube defects, folic acid fortification is associated with a range of additional health benefits across the life course:

- **Prevention of major congenital heart defects** – Large-scale studies show folic acid supplementation may reduce the risk of structural heart defects in newborns (Mao, 2017).

- **Reduction of cleft lip and/or palate** – Folic acid fortification may prevent 40% to 50% of cases, as supported by European cohort data (Wahl, 2015).

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- **Prevention of megaloblastic anemia** – Folic acid helps prevent this form of anemia, especially in working-age adults, improving health and productivity (Green, 2017).
- **Reduced risk of dementia in older adults** – Adequate folate intake may help protect against certain dementias and support healthy aging (Rotstein, 2022).
- **Potential protective effect against pancreatic cancer** – Some evidence suggests folic acid may reduce the risk of pancreatic cancer (Jägerstad, 2012).
- **Reduced risk of stroke and possibly cardiovascular disease** – Large studies show decreased stroke risk and a potential reduction in heart disease with folic acid supplementation (Huo, 2015; Yang, 2024).
- **Arsenic exposure** – A clinical trial in Bangladesh showed that folic acid supplementation reduced blood arsenic levels, suggesting a protective effect in populations exposed to contaminated drinking water (Potera, 2015).

Conclusion

The ISPN strongly supports the use of folic acid fortification at WHO-recommended levels as a **safe, evidence-based, and life-saving intervention**. The scientific community has rigorously reviewed the data on cancer and other potential health effects and has found **no credible evidence** to support any health risk at levels used in food fortification programs.

We encourage all governments, particularly those re-evaluating or considering the adoption of national fortification policies, to rely on the **global scientific consensus** and **the strong body of evidence** supporting the safety and public health benefits of folic acid fortification. For children worldwide, especially in low- and middle-income countries—this remains one of the most effective tools to prevent disability and promote equity in early development.

Our Call to Action

The ISPN calls on governments, policy makers, health professionals, and global health partners to **support the urgent adoption and scale-up of mandatory folic acid fortification policies**. This simple, cost-effective intervention saves lives, prevents severe disability, and contributes to healthier populations.

We stand ready to support countries in implementing evidence-based fortification strategies that protect children and families around the world.

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