What are Neural Tube Defects?

After conception, a neural tube forms within 28 days and develops into the brain and spine\(^1\). Birth defects occur when the neural tube fails to close properly. This can result in neural tissue being exposed and susceptible to damage\(^1\).

The most common neural tube defects (NTDs) are spina bifida, which can lead to permanent disability, and anencephaly which always causes death\(^2\). An estimated 320,000 newborns are affected by NTDs each year worldwide\(^3\).

Why Fortify Flour with Folic Acid?

Most NTDs can be prevented with adequate folic acid intake\(^4,5,6\). The World Health Organization (WHO) recommends that women consume 400 micrograms of folic acid daily, starting from two months before a planned pregnancy through 12 weeks of gestation, to prevent NTDs\(^7\).

Taking folic acid supplements reduces the risk of NTDs\(^8\). However, taking daily supplements requires behavioral change. A review of 49 studies in 22 countries reported that folic acid supplement use was low and inconsistent (ranging from 0.5% in Italy to 52% in the Netherlands)\(^9\). Moreover, approximately half of all pregnancies worldwide are unplanned; women who are not planning a pregnancy may not take supplements during the periconceptional period\(^10\).

Mandatory programs to fortify flour with folic acid have been implemented in at least 80 countries\(^11\). Fortification does not require consumer behavior change, and it improves the folate status of women of childbearing age—before they get pregnant\(^12\). Increasing levels of folic acid in staple foods through fortification increases the likelihood that women will receive adequate amounts of folic acid needed to prevent NTDs\(^13\).

Effectiveness of Fortifying with Folic Acid

A total of 36 studies that compared the prevalence of NTDs before and after large-scale folic acid fortification programs in 13 countries were reviewed (Figure). In these countries, between 1 and 3 milligrams of folic acid were added to each kilogram of wheat flour alone or in combination with maize flour. The prevalence of NTDs before fortification ranged from 3.8 to 43.7 per 10,000 births, which became less variable after flour was fortified with folic acid (3.0-24.3 per 10,000 births). Most studies found a statistically significant decline in the number of NTDs between pre- and post-fortification periods, demonstrating that fortifying flour with folic acid reduced the NTD prevalence.

Studies in the United States have shown declines in the prevalence of overall NTDs (19%-35%) since the implementation of folic acid fortification in 1998\(^14,15,16,17,18,19,42\). Significant decreases in the occurrence of NTDs after folic acid fortification began were also reported in Argentina\(^20,21\), Australia\(^19,41\), Brazil\(^20,22,23\), Canada\(^19,24,25,26,27,28\), Chile\(^26,29,30,31\), Costa Rica\(^32,33\), Iran\(^34\), Jordan\(^35\), Peru\(^36\), Saudi Arabia\(^37\), and South Africa\(^38\).
(1%-78%). The magnitude of the decrease in NTD prevalence varied; countries with higher baseline prevalence had greater declines.

The folate level of women before fortification and the number of women consuming fortified foods, together with the quality of surveillance systems, could affect the decline of NTD prevalence\(^2\). Some researchers found an increase in NTD prevalence post-fortification, yet potential study limitations should be taken into consideration when interpreting the results. A study from Oman showed an 11% increase in the number of overall NTDs, and at the same time showed an 88% decrease in spina bifida\(^3\). One plausible explanation is an improvement in the NTD screening process.

WHO estimates that 5-6 NTDs per 10,000 is the lowest level to be expected after women have optimum folate levels due to folic acid supplementation and/or fortification\(^4\). As noted in the figure below, some studies in Brazil, Canada, Costa Rica, and the USA found the post-fortification NTD level to be 6 per 10,000 or lower. Other studies where more than 6 NTDs per 10,000 were found after fortification indicate room for improving women's folate status at the national or regional level.

In summary, existing evidence suggests that fortifying flour with folic acid contributes to reducing the number of NTDs.

*Figure. A review of 36 documents that reported the prevalence of NTDs per 10,000 births* before and after the initiation of flour fortification with folic acid in 13 countries.*

*The denominator can include live births, still births or terminations.*


