

Vitamins and Neural Tube Defects— Who Benefits?

Research from around the world shows women using multivitamins containing folic acid near the time they become pregnant have less chance of having babies with neural tube defects. Although most studies report multivitamins reduce risk by 50% to 70%, until now, no one has looked at whether they benefit some groups of women more than others.

Over 1000 California women were interviewed in this study by the California Birth Defects Monitoring Program. As in previous reports, those taking multivitamins around conception were less likely to have babies with neural tube defects. However, results were not the same in all groups of women.

MULTIVITAMINS LOWER RISK OVERALL

Women who took multivitamins containing folic acid in the 3 months before or after conception had a lower risk for having infants with neural tube defects. Vitamins did not completely eliminate risk, however—in this study, 60% of women who had affected babies took multivitamins in the first trimester.

- About 1 in 6 women took multivitamins in the 3 months before conception. Women using vitamins had a 35% lower risk than non-users.

- Nearly 7 of 10 women took multivitamins in the first 3 months after conception. On the average, vitamin users had a 40% lower risk.
- Women eating diets with higher levels of folate (the naturally occurring form of folic acid) had lower risk, even if they did not take multivitamins.

These results are for all interviewed women combined. We also examined various subgroups of women and found risk reductions were not equal.

NO BENEFIT IN COLLEGE EDUCATED WOMEN

Taking folic acid-containing multivitamins did not lower risk among women with college degrees. However, women with a high school education or less did benefit from multivitamin use.

LESS BENEFIT IN HISPANICS

In California, Hispanic babies are 50% more likely than White infants to have neural tube defects. Does folic acid decrease the risk?

Nearly half the women interviewed were Hispanic—using folic acid-containing multivitamins lowered their risk only 5% to 25%, much less reduction than was seen in Whites or African-Americans.

SOME FACTS ABOUT NEURAL TUBE DEFECTS AND FOLIC ACID

- Neural tube defects are brain and spine abnormalities found in 1 in 1400 California births, about 400 babies each year. Nationwide, 2500 to 3000 affected babies are born annually.
- These are serious birth defects: spina bifida (open spinal cord) causes lifelong physical disabilities; anencephaly (absence of the brain) leads to infant death.
- The neural tube—the precursor of the brain and spinal cord—develops about 3-4 weeks after conception, often before a woman knows she is pregnant. Although some risk factors are known, causes of neural tube defects are not yet understood.
- Folate is a B-vitamin found in spinach and leafy green vegetables, dried beans, liver, and citrus fruits. In vitamin supplements and fortified foods such as breakfast cereal, it is usually found in the form “folic acid.”
- A number of studies worldwide report that taking multivitamins containing folic acid around the time of conception lowers the neural tube defect risk. The average risk reduction is around 50%.
- For this reason, the US Public Health Service now recommends all women of childbearing age take a supplement containing 0.4 milligrams of folic acid daily.



TIMING, DOSE, AND OTHER FACTORS

- The risk reduction was similar whether multivitamin use began before conception, in the first trimester, or later in pregnancy.
- Daily folic acid intake—from diet and multivitamins combined—was linked to risk reduction. As total folic acid intake increased, risk decreased.
- Reduced risk with multivitamin use was seen for both main types of neural tube defects—spina bifida and anencephaly—whether isolated or accompanied by other major birth defects.

We examined several other variables such as smoking, mother’s age and number of past pregnancies, whether or not she used prenatal diagnosis. These factors correlated strongly with the mother’s education, as did the risk reductions seen in these categories.

CLARIFIES EARLIER CALIFORNIA STUDY

Published in 1989, the only large study to date not showing lowered risk with multivitamin use was based on interviews with California and Illinois women. Our study shows that, in California, different groups of women benefit unequally from multivitamins. In the 1989 study, if selection criteria favored one group—for example, those with college degrees—results may have been skewed. Biased selection is unlikely to be a limitation in our population-based study.

There are other possible sources of bias. Women’s recall of events in early pregnancy may be swayed by their beliefs about birth defects causes. To test this, we asked women in the study if they thought vitamins caused birth defects, prevented them, or had no effect. We saw similar risk regardless of response, suggesting that recall bias is not a factor.

RECOMMENDATIONS

On the average, multivitamins containing folic acid reduce neural tube defects risk, although some women benefit more than others. Even among the groups with no reduction *on the average*—for instance, those with college degrees—there undoubtedly are *individual* women who do benefit. Currently there is no way to identify these women. For this reason, we advise all women to follow current recommendations regarding folic acid use: take 0.4 milligrams daily. This is particularly important before conception and in very early pregnancy..

COMPREHENSIVE STUDY DESIGN

Testing a number of hypotheses about possible causes and risk factors, this is the most extensive ever case-control interview study of neural tube defects.

- **Participants:** A very high proportion of mothers contacted—88%—agreed to be interviewed: 549 mothers of infants/fetuses with neural tube defects and 540 mothers of infants without birth defects. All deliveries occurred in 1989-1991. 43% of mothers interviewed were Hispanic; 83% of these were of Mexican descent.
- **Diagnostic information:** Abstracted from hospital medical records, including surgical and autopsy reports.
- **Interview:** Conducted in the mother's home by a trained interviewer, in English or Spanish, 3-6 months after the baby's due date. The 2.5-hour structured survey asked about events and exposures before and during pregnancy,

beliefs about birth defects causes, family history, and demographics.

- **Folic acid intake:** Estimated from questions about vitamin/mineral supplement composition and frequency of use. We assessed dietary consumption separately in over 1000 women who completed a detailed food frequency questionnaire. They reported eating habits and serving sizes for 100 foods.

FUTURE RESEARCH

These are the first results from the most comprehensive study to date on neural tube defects. The extensive interview explored a number of possible exposures and other factors which may cause or protect against this serious condition. Future data analysis will provide more answers, particularly for those women not helped by folic acid. The understanding gained from research like this will ultimately prevent birth defects.

REFERENCE: Shaw GM, Schaffer D, Velie EM, Morland K, Harris JA. Periconceptional vitamin use, dietary folate, and the occurrence of neural tube defects. Epidemiology 1995; 6(3):219-226.

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