

Folic Acid May Prevent Cleft Lip and Palate

A new study finds that women who take folic acid supplements early in their pregnancy can substantially reduce their baby's chances of being born with a facial cleft.

Researchers at the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health, found that 0.4 milligrams (mg) a day of folic acid reduced by one third the baby's risk of isolated cleft lip (with or without cleft palate). Folic acid is a B vitamin found in leafy vegetables, citrus fruits, beans, and whole grains. It can also be taken as a vitamin supplement, and it is added to flour and other fortified foods. The recommended daily dietary allowance for folate for adults is 400 micrograms or 0.4 mg.

"These findings provide further evidence of the benefits of folic acid for women," said Allen J. Wilcox, M.D., Ph.D., lead NIEHS author on the new study published online in the *British Medical Journal*. "We already know that folic acid reduces the risk of neural tube defects, including spina bifida. Our research suggests that folic acid also helps prevent facial clefts, another common birth defect." In the United States, about one in every 750 babies is born with cleft lip and/or palate.

"Folic acid deficiency causes facial clefts in laboratory animals, so we had a good reason to focus on folic acid in our clefts study," said Wilcox. "It was one of our main hypotheses."

The researchers examined the association between facial clefts and mothers' intake of folic acid supplements, multivitamins, and folates in diet. The researchers found that folic acid supplementation of 400 micrograms or more per day reduced the risk of isolated cleft lip with or without cleft palate by one-third, but had no apparent effect on the risk of cleft palate alone.

"A mother's nutrition during pregnancy is clearly an environmental factor that can affect the health of her fetus," said NIEHS Director David A. Schwartz, M.D. The NIEHS researchers are continuing to analyze their data for evidence of other environmental exposures that increase the risk of facial clefts.

This population-based study was conducted in Norway, which has one of the highest rates of facial clefts in Europe and does not allow foods to be fortified with folic acid. The investigators contacted all families of newborn infants with clefts (either cleft lip with or without cleft palate (CLP) or cleft palate only (CPO)) born between 1996 and 2001 in Norway. The study included 377 babies with CLP and 196 with CLO; as well as 763 control babies randomly selected from all live births in Norway.

The researchers mailed two questionnaires to each of the mothers participating in the study. The first questionnaire mailed soon after delivery focused on general health information, including demographics, reproductive history and information about environmental exposures including smoking, alcohol and vitamins; whereas the second

questionnaire focused on nutrition and diet during the pregnancy. Mothers who reported taking folic acid supplements and or multivitamins were asked to send in their empty bottles or labels to confirm dosage.

The nutrition questionnaire included questions on mothers' fruit and vegetable consumption during the first three months of pregnancy.

The researchers estimated that 22 percent of isolated CLP cases in Norway could be averted if all pregnant women took 0.4 mg of folic acid per day.

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Reference: Wilcox AJ, Lie RT, Solvoll K, Taylor J, McConnaughey DR, Abyholm F, Vindenes H, Vollset SE, Drevon CA. "Folic Acid Supplements and the risk of facial clefts: A National population-based control study." *British Medical Journal*, 2007