

Low levels of vitamin B12 may increase risk for neural tube defects

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Children born to women who have low blood levels of vitamin B12 shortly before and after conception may have an increased risk of a neural tube defect, according to an analysis by researchers at the National Institutes of Health, Trinity College Dublin, and the Health Research Board of Ireland.

Women with the lowest B12 levels had 5 times the risk of having a child with a neural tube defect compared to women with the highest B12 levels.

Women who consume little or no meat or animal based foods are the most likely group of women to have low B12 levels, along with women who have intestinal disorders that prevent them from absorbing sufficient amounts of B12.

Neural tube defects are a class of birth defects affecting the brain and spinal cord. One type, spina bifida, can cause partial paralysis. Another type, anencephaly, is a fatal defect in which the brain and skull are severely underdeveloped.

Researchers have known that taking another nutrient, folic acid, during the weeks before and after conception can greatly reduce a woman's chances of having a child with a neural tube defect. Folic acid is the synthetic form of the vitamin folate. In the United States, cereal grains are fortified with folic acid to reduce the occurrence of neural tube defects in the U.S. population.

The study appears in the March *Pediatrics*. The study's first author was Anne M. Molloy, Ph.D., Trinity College Dublin. Scientists from the Health Research Board of Ireland and two NIH institutes, the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Human Genome Research Institute, also took part in the study.

"Vitamin B12 is essential for the functioning of the nervous system and for the production of red blood cells," said Duane Alexander, M.D., director of the NICHD. "The results of this study suggest that women with low levels of B12 not only may risk health problems of their own, but also may increase the chance that their children may be born with a serious birth defect."

Ireland has a high rate of neural tube defects, and NIH scientists have frequently collaborated with Irish researchers to gain insight into the causes of this group of disorders.

To conduct the study, the researchers analyzed stored blood samples originally collected during early pregnancy from three groups of Irish women between 1983 and 1990. During that time, pregnant women in Ireland rarely took vitamin supplements. The study authors reasoned that the lack of routine vitamin supplementation would allow them to identify a sufficient number of women with low Vitamin B12 to conduct their analysis.

For their analysis, the researchers classified the women into three groups. The first group consisted of 95 women who were pregnant with a child having a neural tube defect at the time the blood was taken. The second group was composed of 107 women who had previously given birth to a child with a neural tube defect but whose current pregnancy was not affected. Like the first group, women in the third group (a total of 76) were pregnant with a child having a neural tube defect at the time

the blood sample was obtained, but were enrolled in a different study than the women in group 1. The researchers measured the Vitamin B12 and folate levels of the women's blood samples, and compared them to those of control groups whose pregnancies were unaffected by a neural tube defect.

Because low folate levels are a known risk factor for neural tube defects, the researchers used statistical techniques to evaluate the role of Vitamin B12 independently of the role of folate. In all three groups, women with low B12 concentrations (estimated at less than 250 ng/L, before pregnancy) had 2.5-3 times the risk of having a child with a neural tube defect compared to those with higher levels. Women with levels in the deficient range (0-149 ng/L) were at the highest risk: 5 times that of women with higher levels.

The study authors wrote that it is not known how B12 and folate might interact to influence the formation of the neural tube, the embryonic structure that gives rise to the spine and brain. They noted that the two vitamins are jointly involved with several key biochemical reactions, as well as with the synthesis of DNA. Lack of either Vitamin B12 or folate in any of these chemical processes theoretically could increase the risk of a neural tube defect.

The authors noted that their results needed to be confirmed by other studies among other populations of women. They suggested, however, that women should have Vitamin B12 levels above 300 ng/L before becoming pregnant. (Because B12 levels drop sharply during pregnancy, the researchers adjusted the levels measured during pregnancy to provide a target level for women to achieve before they become pregnant.)

Because Vitamin B12 comes from foods of animal origin, women who adhere to a strict vegan diet may be at risk for a B12 deficiency, said an NICHD author of the paper, James L. Mills, M.D., senior investigator in

the Division of Epidemiology, Statistics, and Prevention Research. He added it is advisable for women with digestive disorders that interfere with the absorption of foods to consult a physician before getting pregnant, to make sure they are receiving adequate amounts of B12.

Dr. Mills explained that critical events in the formation of the brain and spinal column occur very early in pregnancy—in the first 28 days after conception—before many women even realize they are pregnant.

He added that the U.S. Public Health Service recommends that all women of childbearing age consume 400 micrograms of folic acid each day. This amount assures that a woman will have adequate stores of the vitamin, in the event of an unintended pregnancy.

"If women wait until they realize that they are pregnant before they start taking folic acid, it is usually too late," Dr. Mills said.

Similarly, he said, it would be wise for all women of childbearing age to consume the recommended amount of Vitamin B12, whether they are planning a pregnancy or not. "Half of the women who become pregnant each year in the U.S. were not planning to become pregnant."

"Our results offer evidence that women who have adequate B12 levels before they become pregnant may further reduce the occurrence of this class of birth defects," Dr. Mills said.

More information: Vitamin B12 is available in milk, meats, poultry, eggs, as well as fortified cereals and some other fortified foods. Information on foods that contain Vitamin B12, as well as the Recommended Dietary Allowances for the vitamin, is available from the NIH Office of Dietary Supplements, dietary-supplements.info.nih.gov/...heets/vitaminb12.asp.

Source: NIH/National Institute of Child Health and Human Development

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