B_{12} Level May Predict Neural Tube Defect Risk

BY ELIZABETH MECHCATIE

A low vitamin B_{12} blood level was an independent and significant risk factor for having a pregnancy affected by a neural tube defect in a study of Irish women, in what the authors say is the first study to examine the risk of the birth defect associated with maternal B_{12} concentration.

Their results have public health implications in terms of possible fortification of grains with B_{12}, although studies are needed to learn more about the safety of this approach and the optimal protective dose of B_{12} in food, according to Anne M. Molloy, Ph.D., of Trinity College, Dublin and her associates.

The data indicated that most of neural tube defect (NTD) risk was limited to maternal B_{12} levels of approximately 250 ng/L or less, with the possibility that the risk could be further lowered if the B_{12} level was above 320-350 ng/L, the authors noted. Based on these findings, they recommended that women have a vitamin B_{12} level above 300 ng/L before conceiving (Pediatrics 2009;123:917-23).

The other investigators were from the Health Research Board in Dublin and the National Institutes of Health. Because the neural tube defect rate in Ireland is high, NIH and Irish researchers have worked together on NTD studies.

The study compared B_{12} levels in stored blood samples of three groups of Irish women, at a median 15 weeks' gestation, obtained between 1983 and 1990, before food was fortified with folic acid and when vitamin supplementation during pregnancy in Ireland was not common. Mandatory folic acid fortification of grains in the United States has reportedly reduced the incidence of NTDs by as much as 78%. But folic acid cannot prevent all NTDs and low maternal B_{12} has previously been associated with a risk of NTDs, the authors wrote.

The three groups were composed as follows: 95 women with a pregnancy affected by a NTD (mean age 27 years) and 265 controls with a normal pregnancy (mean age 28 years); 107 women who had had a previous pregnancy affected by an NTD but were pregnant again with an unaffected pregnancy (mean age 32 years) and 414 controls (mean age 28 years); and 76 women during an affected pregnancy (mean age 27 years) and 222 controls (mean age 28 years).

The analysis of stored blood samples obtained at a median 15 weeks' gestation suggested that women have a vitamin B_{12} level above 300 ng/L before conceiving.

When compared with controls, the B_{12} levels were significantly lower among the women who had a pregnancy affected by a NTD, with levels below 250 ng/L associated with the greatest risk. The risk of having a pregnancy affected by an NTD was three times greater among women with B_{12} concentrations below 200 ng/L, compared with those whose levels were above 400 ng/L.

Median B_{12} concentrations among the affected women in all groups were 13%-19% lower than those with unaffected pregnancies, a significant difference.

Since B_{12}values were obtained at a median 15 weeks' gestation, at which time the level naturally would have dropped by about 20%-25%, "our data indicate that women should aim to enter pregnancy" with serum B_{12} concentrations above 300 ng/L," the authors concluded, adding that concentrations above 400 ng/L "might be desirable, although we found no statistically significant benefit," for that value.

The researchers did an analysis to determine if the effects of B_{12} and folate on NTD risk were independent, which found "little interaction between B_{12} and folate," they said. Mandatory fortification of grain products in the United States with folic acid, the synthetic version of the vitamin folate, has been reported to reduce NTD incidence by as much as 78%. But, "it is generally agreed that not all NTDs are preventable by folic acid," according to the investigators, who had no relevant disclosures. ■