

Shaw GH, et al. Choline and risk of neural tube defects in a folate-fortified population, *Am J Epidemiol* 2009;20:714-9.

Background: Folic acid is known to reduce risk of neural tube defects (NTDs). Even so, NTDs continue to occur despite individual supplementation or population fortification with folic acid. We investigated other nutrients related to one-carbon metabolism that may affect NTD risk.

Methods: This prospective study included data from more than 180,000 pregnant women in California from 2003 through 2005. Midpregnancy serum specimens were linked with delivery information regarding the presence of a NTD, another structural malformation, or no malformation in the fetus. We identified 80 NTD-affected pregnancies (cases) and we randomly selected 409 pregnancy controls. Serum specimens were tested for methylmalonic acid, homocysteine, cysteine, methionine, total choline, betaine, cystathionine, vitamin B6, folate, vitamin B12, riboflavin, and creatinine.

Results: We observed elevated NTD risks associated with lower levels of total choline, and reduced risks with higher levels of choline. Specifically, we observed an odds ratio of 2.4 (95% confidence interval 1.3–4.7) associated with the lowest decile and an odds ratio of 0.14 (0.02–1.0) associated with the highest decile, both relative to the 25th–74th percentiles of the control distribution. These data did not show meaningful differences between cases and controls for any other analytes.

Conclusions: This is the first study to investigate total choline in NTD-affected pregnancies. Our findings for choline, for which low levels were a risk factor and higher levels were a protective factor for NTDs, may offer a useful clue toward understanding the complex etiologies of NTDs in an era of folic acid fortification of the food supply.