

## Letter to the Editor

# Folic Acid and Miscarriage: An Unjustified Link

### To the Editor:

The letter by Windham et al., [2000] cannot be taken as showing that folic acid causes miscarriage, and Professor Hook's interpretation of the results to this effect in his editorial comment [Hook, 2000] is unjustified.

Windham and her colleagues compare the rates of miscarriage in women who took multivitamins early in pregnancy with women who did not. The rates were, respectively, 10.3% and 9%, a difference that was not statistically significant (reported relative risk 1.14, with a 95% confidence interval of 0.96–1.36). In his editorial, Professor Hook gives a *P* value for this difference of 0.06 but this is based on a one-tailed test, which is inappropriate. Even if there were a result that could not be explained by chance, there would be no reason to conclude that this was due to folic acid because many other vitamins were included in the multivitamin preparation.

The MRC Vitamin Study [Wald et al., 1991] is the only large randomized, controlled trial capable of examining the specific effect of folic acid on miscarriage, and overall it provided no suggestion of an effect (relative risk of 1.06 with a 95% confidence interval of 0.79–1.43, *P* = 0.70) [Wald and Hackshaw, 1997]. If the data were restricted to compare those women who were only given folic acid with those given neither folic acid nor

multivitamins, the relative risk is 0.98 (95% confidence interval 0.64–1.49, *P* = 0.91). There is not even a suggestion that folic acid supplementation is a cause of miscarriage. The negative evidence is all the more compelling given that the MRC trial used a high dose of folic acid (4 mg), approximately 10 times greater than that used in supplements available over the counter.

### REFERENCES

- Hook EB. 2000. Folic acid: abortifacient or pseudoabortifacient? *Am J Med Genet* 93:301–302.
- Wald NJ, Hackshaw AK. 1997. Folic acid and prevention of neural tube defects. *Lancet* 350:665.
- Wald N, Sneddon J, Densem J, Frost C, Stone R. 1991. Prevention of neural tube defects: results of the MRC vitamin study. *Lancet* 338:132–137.
- Windham GC, Shaw GM, Todoroff K, Swan SH. 2000. Miscarriage and the use of multi-vitamins or folic acid. *Am J Med Genet* 90:260–262.

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