High Folate Hikes Odds of Twinning After IVF

BY MARY ANN MOON
Contributing Writer

A high plasma folate level around the time of conception raises the chance of twinning after in vitro fertilization, but not the chance of having a successful pregnancy, reported Paul Haggarty, Ph.D., of the Rowett Research Institute, Aberdeen, Scotland, and his associates.

"Our results suggest that the high incidence of twin births associated with treatment for infertility could be reduced, while maintaining [live birth] rates, by encouraging women not to exceed recommended doses of folic acid and by identifying those at high risk of twins after double-embryo transfer on the basis of their plasma folate concentrations and age," they wrote (Lancet 2006;367:1513-9).

"The need to increase the intake of folic acid to reduce the incidence of neural tube defects is not in doubt, but the associated risks of multiple births after IVF need to be addressed," they noted.

High folate levels have been associated with an increase in natural twinning, and "there are good biological reasons to suspect that B-vitamin exposure" also affects twinning in IVF pregnancies. Dr. Haggarty and his associates assessed vitamin B intake, plasma and red cell levels of folate, and six variants in genes known to be involved with B-vitamin metabolism in 602 women undergoing IVF. For comparison, they also performed the same genetic analysis in 932 women who had conceived naturally and had singleton pregnancies.

Folate and vitamin B intake correlated with plasma and red-cell levels of folate. Neither one was associated with the rate of live births or the rate of pregnancy loss after IVF. However, both were associated with an increased rate of twinning in the IVF group.

Younger maternal age also was associated with an increased rate of twinning.

Women in the United Kingdom who are trying to conceive either naturally or through IVF are advised to take 400 mcg of supplementary folic acid daily before and after conception, to reduce the risk of neural tube defects. But flour and other foods are not fortified with folate in the United Kingdom as they are in the United States. If they were, the average daily intake of folate would increase another 200 mcg in the United Kingdom, which would translate into an additional 600 IVF twin births there every year, the researchers said.

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This is consistent with the 11%-13% increase in the rate of multiple births after IVF that was observed in the United States when folic acid fortification was mandated by the Food and Drug Administration in 1998, Dr. Haggarty and his associates added.

In an editorial comment accompanying this report, Dr. Gary Steinman of the department of ob.gyn. at Albert Einstein College of Medicine, New York, said that the mechanism underlying this association between folate and twinning still remains to be explained.

It may involve serum levels of insulin-like growth factor (IGF). Cows that have been crossbred to enhance their spontaneous twinning rate show twice the average serum levels of IGF, and human vegans—whose IGF levels typically are 13% lower than those in the general population—have a twinning rate that is comparably lower than the rate in vegetarians and omnivores, he said (Lancet 2006;367:1461-2).

Studies in ethnic populations also support an association between diet, serum IGF level, and twinning. The Yoruba women living in rural Nigeria have an unusually high twinning rate that is attributed to their high consumption of yams, which significantly raises their serum IGF levels. When they move to the city and change their diets, their IGF levels drop significantly, as does their twinning rate. Similarly, Japanese women have one of the lowest twinning rates of any ethnic group, but when they relocate to the United States and change their diets, their serum IGF rises dramatically and their twinning rate doubles, Dr. Steinman noted. ■