

Study links dietary folate intake to genetic abnormalities in sperm

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Healthy men who report lower levels of the nutrient folate in their diets have higher rates of chromosomal abnormalities in their sperm, according to a new study by researchers at the University of California, Berkeley, and the Lawrence Berkeley National Laboratory.

Women of child-bearing age are encouraged to maintain adequate levels of folate in their diet, but the new findings, to be published Thursday, March 20, in the journal *Human Reproduction*, provide evidence that what men eat may also affect reproductive health.

"Recent studies have suggested that paternal diet affects sperm count and motility, which is important for conception, but this new study takes it further to say that male diet may be important for healthy offspring as well," said study coordinator Suzanne Young, a researcher at UC Berkeley's School of Public Health. "Our study is the first to look at the effects of diet on chromosomal abnormalities in sperm. These abnormalities would cause either miscarriages or children with genetic syndromes if the sperm fertilized an egg."

Folate is a water-soluble B vitamin that occurs naturally in a wide range of foods, particularly liver, leafy green vegetables, citrus fruits and legumes. It is needed during the synthesis of DNA, RNA and proteins, and it is necessary for the production of new cells. Folate also helps keep in check levels of homocysteine, an amino acid that, when elevated, is linked to heart disease.

Studies have shown that adequate intake of folate by women just before and during pregnancy significantly reduces the risk of neural tube birth defects, such as spina bifida or anencephaly.

To ensure that women get the recommended daily intake of 400 micrograms of folic acid, the synthetic form of folate, and reduce the risk of these birth defects, the U.S. government in 1998 began requiring food manufacturers to add folic acid to breads, cereals, flours and other grain products. At least one study suggests that there has been a significant reduction in neural tube birth defects in this country since the folic acid fortification program began.

"The emphasis related to the birth of a healthy baby has been weighted towards the health and diet of women, not just during pregnancy, but before," said Brenda Eskenazi, professor of epidemiology and maternal and child health at UC Berkeley's School of Public Health and co-principal investigator of the study. "What we're finding now is that a nutritious diet, specifically folate intake, may be beneficial for men as well when it comes to producing healthy offspring."

An estimated 1 to 4 percent of a healthy male's sperm have abnormal numbers of chromosomes, or aneuploidy, that are caused by errors during cell division (meiosis) in the testis. However, the causes of these errors are not well understood. If these abnormal sperm fertilize a normal egg, there would either be a miscarriage or a fetus with a chromosomal disorder such as trisomy, in which cells have three rather than the normal two copies of a given chromosome.

For this study, the researchers targeted three chromosomes - X, Y and chromosome 21 - because they are associated with common types of aneuploidy in live births. For example, children born with an extra chromosome 21 have Down syndrome, characterized by mild to severe mental retardation, while boys with an extra X chromosome have

Klinefelter syndrome, which could affect language and learning development. Boys with an extra Y chromosome, or XYY syndrome, may also have some learning and behavioral difficulties.

The researchers studied 97 men who were ages 22 to 80 and who worked at or had retired from a government research laboratory. The study excluded smokers and those with previous or existing reproductive or fertility problems.

Researchers determined average intake of dietary and supplemental nutrients, including multi-vitamins, through participant questionnaires. Semen samples were collected within a week of completing the questionnaires.

After accounting for factors such as age, alcohol use and medical history, the researchers found that men reporting the highest intake of folate had 19 percent lower rates of sperm with abnormal numbers of chromosomes than men with moderate folate intake, and 20 percent lower rates compared with men in the low folate intake group.

The researchers were not able to determine a link between sperm aneuploidy and the other nutrients examined, such as zinc, calcium, beta-carotene and other vitamins.

But before fathers-to-be start popping folic acid supplements, the researchers caution that this study only found a link, not a cause-and-effect relationship, between folate and chromosomal abnormalities.

"We can't yet say that increasing folate in your diet will lead to healthier sperm," said study co-principal investigator Andrew Wyrobek, chair of the Radiation Biosciences Department at Lawrence Berkeley National Laboratory. "But we did come up with enough evidence to justify a larger, clinical and pharmacological trial in men to examine the causal

relationships between dietary folate levels and chromosomal abnormalities in their sperm. This information will help us set dietary folate levels that may reduce the risk of miscarriage or birth defects linked to the fathers."

If future studies verify higher folate intake with lower rates of sperm abnormalities, it may be worthwhile to increase the U.S. recommended daily allowance of folate for men considering fatherhood from the current level of 400 micrograms per day, the researchers said.

Source: University of California - Berkeley

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