Medical Xpress

Zinc deficiency before conception disrupts fetal development

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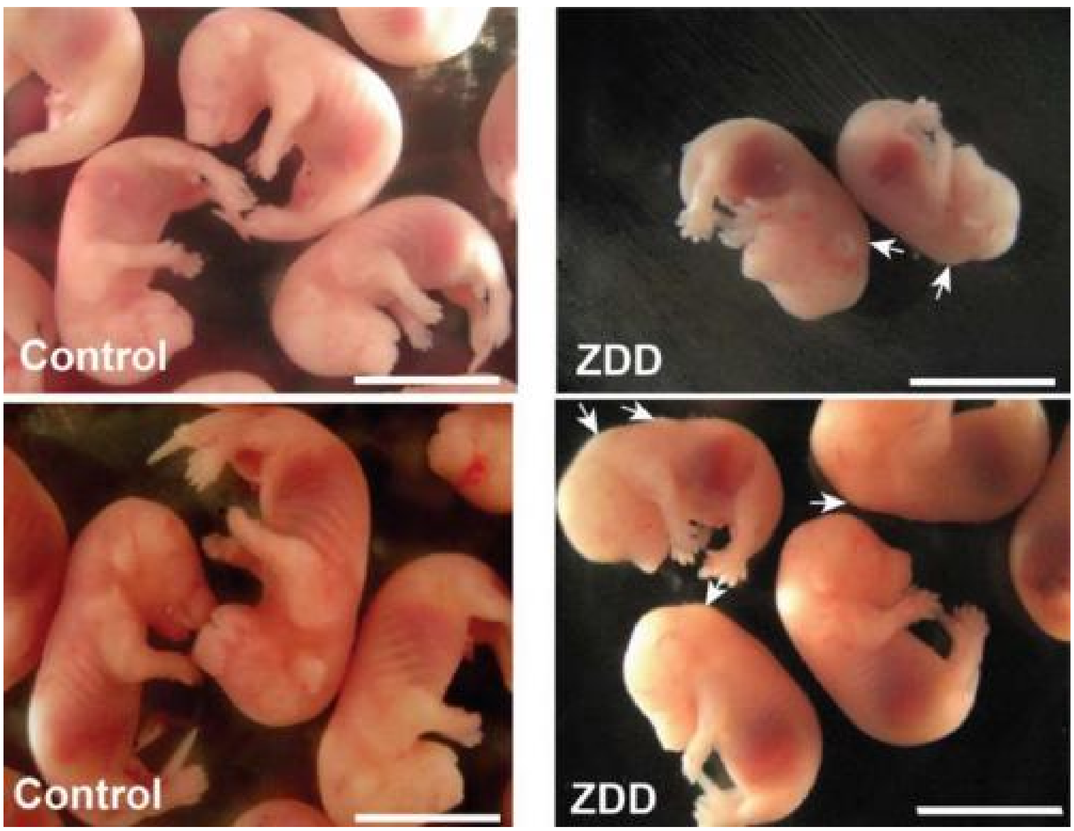


Fetuses from zinc-deficient mice in the study were 38 percent smaller on average than those from the control group fed a diet with zinc included. Credit: Penn State

Female mice deprived of dietary zinc for a relatively short time before conception experienced fertility and pregnancy problems and had smaller, less-developed fetuses than mice that ingested zinc during the same times, according to researchers in Penn State's College of Agricultural Sciences.

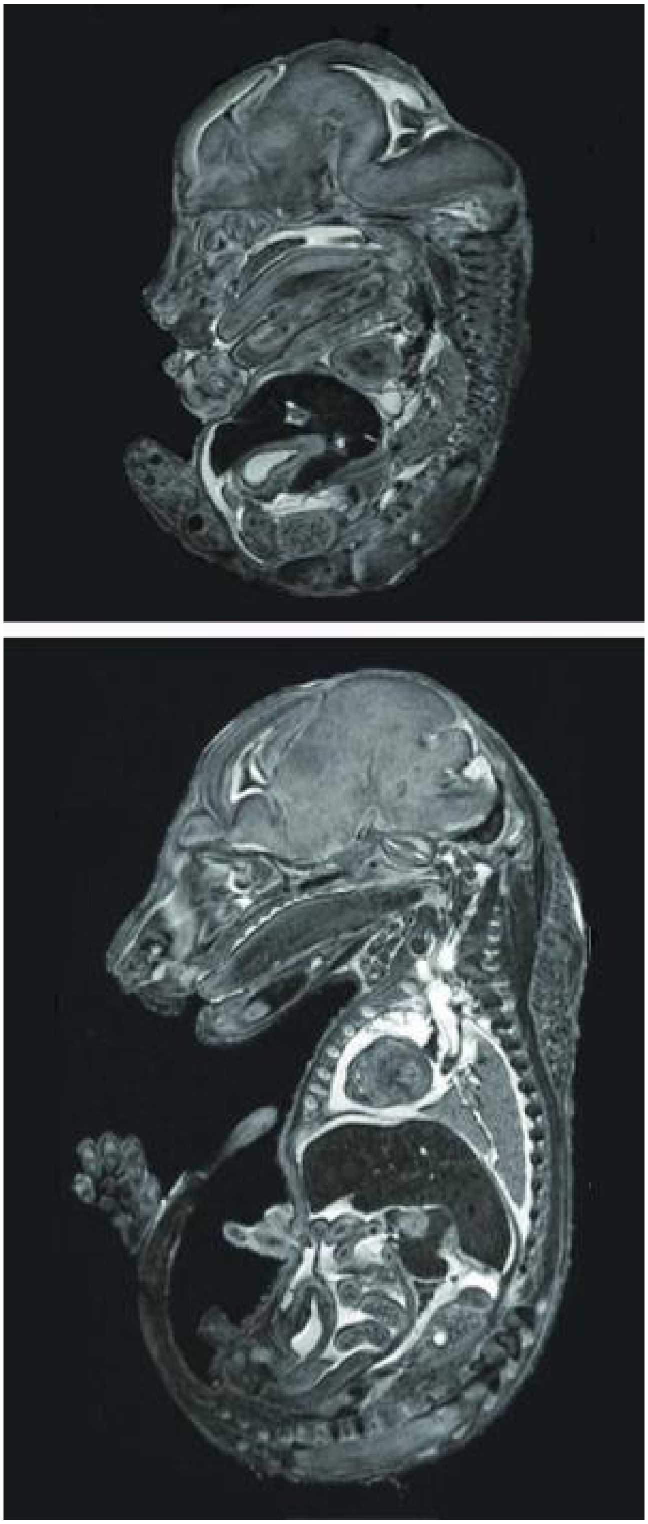
The findings have implications for human reproduction, scientists suggest.

Going without zinc prior to ovulation had marked effects on the mice's reproductive functions. Zinc deficiency caused a high incidence of pregnancy loss, and embryos from the zinc-deficient diet group were an average of 38 percent smaller than those from the control group. Preconception zinc deficiency also caused approximately half of embryos to exhibit delayed or aberrant development.

Defects in placenta development are a major cause of delayed embryo/fetal development because the developing embryos do not get enough nutrients to support normal growth. In the zinc-deficient group, the fetal side of the placenta was much less developed. Consistent with delayed development of the placenta, expression of key placental genes was sharply curtailed in mice with zinc-deficient diets.

Collectively, the findings provide evidence for the importance of preconception zinc in promoting optimal fertility and embryo, fetal and placenta development, explained Francisco Diaz, assistant professor of reproductive biology.

"The mineral zinc acts as a catalytic, structural and signaling factor in the regulation of a diverse array of cellular pathways involving hundreds of enzymes and proteins," he said. "Given these wide-ranging roles, it is not surprising that insufficient zinc during pregnancy causes developmental defects in many species. We have known that for a long time.



Magnetic resonance images of two mouse fetuses -- the top is a smaller, malformed one from a zinc-deficient mouse; the bottom is a healthy fetus from a mouse in the control group. Credit: Penn State

"However, the role of zinc during the preconception period in promoting later development during pregnancy is not clearly understood."

In the six-month study, which was published online in a recent edition of *Biology of Reproduction*, female mice were fed a control or a zinc-deficient diet for four to five days before ovulation. Then, embryonic and/or placental development was evaluated on days three, six, 10, 12 and 16 of pregnancy.

At each of those intervals, Xi Tian, recent Penn State doctoral student and now a postdoctoral scholar at the University of North Carolina, Chapel Hill, measured and evaluated fetuses, examining them with light microscopy and magnetic resonance imaging. She was assisted by co-authors Thomas Neuberger, assistant professor of biomedical engineering in Penn State's Huck Institutes of Life Sciences, working with the Penn State's High-Field Magnetic Resonance Imaging Facility, and Kate Anthony, research technician in animal science.

"What these results demonstrate is that a relatively short dietary disruption in nutrients that are available can have an impact on the ovary, the quality of the egg that the ovary produces, and the quality of the embryo and placenta that the egg develops into after fertilization," Diaz said. "We know that dietary restrictions can have an effect on pregnancy and on fetal and placental development, but we are not as familiar with preconception effects that are relatively acute and then seeing the effect later on in pregnancy. That is the most novel aspect of our work here."

One way that zinc may affect egg development is by promoting the epigenetic programming of the DNA of the oocyte, or immature egg cell. During egg development, "methyl groups," or chemical tags, are added at specific locations on the DNA and are essential for that egg to fully support embryo and placenta development later on.

"We found much less DNA methylation in eggs from zinc deficient mice, suggesting that programming of the egg is defective," Diaz said.

Diaz noted that this research and follow-up studies may result in a recommendation for women intending to get pregnant to make a special effort to eat foods containing zinc in the weeks prior to ovulation, or even to take zinc supplements. Foods containing higher levels of zinc include meats, seafood and milk. Fruits and vegetables contain lower amounts of the mineral.

"It looks like zinc is similar to folic acid, which is one of the few nutrients that are prescribed before a woman becomes pregnant, because it is needed preconception to ensure the quality of the egg," Diaz said. Zinc is very similar in that it is needed before conception—so giving multivitamins or supplements to a woman after she has found out that she's pregnant doesn't really address the issue."

"It is certainly important during pregnancy, but if the egg development is already compromised, it may not help that aspect of development. I think our work suggests that you need zinc preconception, just like you need folic acid."

A woman's requirement for zinc is not large—unlike for calcium or iron—but there is a fairly rapid turnover of zinc in the body, so humans need a steady supply, Diaz pointed out.

"Actually, our mice become zinc deficient rather quickly," he said. "Animal studies have shown that some tissues can become zinc deficient within a few days."

Provided by Pennsylvania State University