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Genome-wide DNA study shows lasting impact of malnutrition in early pregnancy

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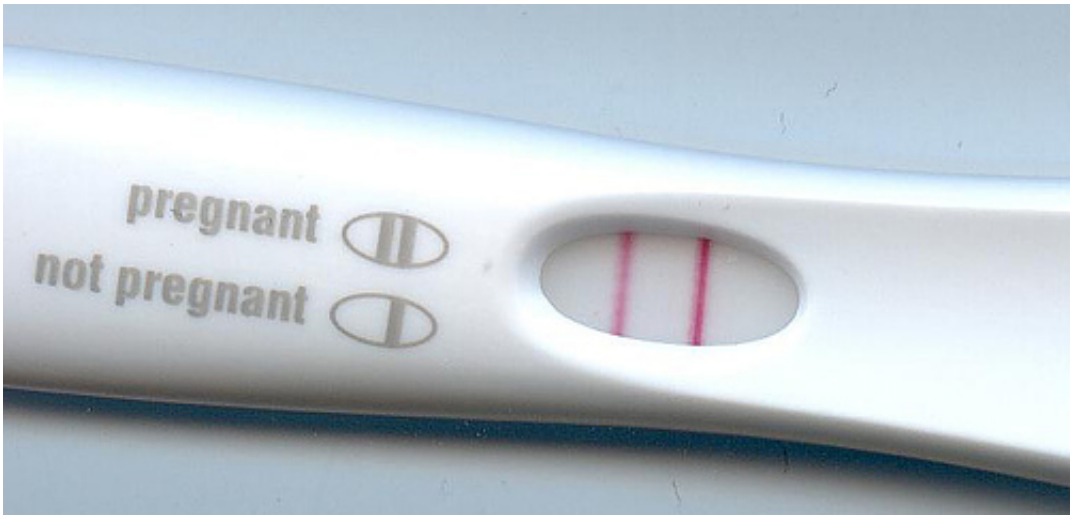

Pregnancy test. Credit: public domain

Researchers at Columbia University's Mailman School of Public Health and Leiden University in the Netherlands found that children whose mothers were malnourished at famine levels during the first 10 weeks of pregnancy had changes in DNA methylation known to suppress genes involved in growth, development, and metabolism documented at age 59. This is the first study to look at prenatal nutrition and genome-wide DNA patterns in adults exposed to severe under-nutrition at different periods of gestation. Findings are published in the *International Journal of Epidemiology*.

The study evaluated how famine exposure—defined as 900 calories daily or less—during the Dutch Hunger Winter of 1944-1945 affected genome-wide DNA methylation levels. The researchers also studied the impact of short-term exposure, pre-conception and post-conception. The study used blood samples of 422 individuals exposed to the famine at any time during gestation and 463 controls without prenatal famine exposure.

The authors examined individuals born between February 1945 and March 1946 whose mothers were exposed to the famine during or immediately preceding pregnancy, individuals conceived between March and May 1945 at the time of extreme famine, and controls born in the same institutions whose mothers did not experience famine while pregnant as well as sibling controls who were also not exposed to famine in pregnancy.

The findings show associations between famine exposure during weeks 1-10 of gestation and DNA changes, but not later in pregnancy. DNA methylation changes were also seen among individuals conceived at the height of the famine between March and May 1945 who were not exposed to all 10 weeks of early gestation. "The first ten weeks of gestation is a uniquely sensitive period when the blood methylome—or whole-genome DNA methylation—is especially sensitive to the prenatal environment," said L.H. Lumey, MD, PhD, associate professor of Epidemiology at the Mailman School of Public Health, and last author. "This is the period when a woman may not even be aware that she is pregnant."

Earlier studies in other populations in the Netherlands led by Dr. Lumey examined the long-term impact of famine exposure and identified early gestation as the most critically sensitive period. Their work among over 45,000 military recruits revealed that famine exposure in the first pregnancy trimester was associated with a 10-percent increase in

mortality at age 63 years.

Ongoing Research

"Further analysis of health outcomes among men and women with famine exposure is now needed. We are therefore looking if DNA-methylation can make a difference for obesity and diabetes risk in this population," said Lumey. "We are also interested in sex-specific effects, but for these questions larger studies may be needed."

Provided by Columbia University's Mailman School of Public Health