How do stress hormones during pregnancy predict adult nicotine addiction?

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Adult women whose mothers had increased levels of stress hormones while they were pregnant are at greater risk of becoming addicted to nicotine, according to a new study led by a Miriam Hospital researcher.

The 40-year longitudinal study provides the first evidence that prenatal exposure to the class of stress hormones known as glucocorticoids predicts nicotine dependence later in life – but only for daughters. It also confirms previous research that babies born to moms who smoked when pregnant have an increased risk of nicotine addiction in adulthood.

The study found that effects of maternal stress hormones and maternal smoking in pregnancy were additive in predicting nicotine addiction in adult daughters. The findings, published online by the journal *Biological Psychiatry*, point to the enduring influence of the prenatal environment and the importance of maternal health and well-being during pregnancy.

Lead author Laura Stroud, Ph.D., from the Centers for Behavioral and Preventive Medicine at The Miriam Hospital, says the study supports the critical role of the prenatal environment when it comes to risk factors for adult disease, meaning some people may be predisposed to, or 'programmed' for, certain conditions later in life because of exposures during pregnancy, such as stress and maternal smoking.

"While maternal smoking during pregnancy has been shown to be an independent risk factor for nicotine dependence, we didn't really know – until now – which pathways or mechanisms were responsible. Most prior research involving biological mechanisms had been conducted in animals not humans," she said.

"Our study suggests that maternal smoking and high stress hormones—often linked to high stress and adverse social conditions—represent a 'double-hit' in terms of increasing an offspring's risk for nicotine addiction as an adult." Because mothers who smoke are often more stressed and living in adverse conditions—these findings represent a public health concern and highlight the need to help smoking moms quit and reduce stress levels and improve social conditions for poor pregnant mothers," Stroud added.

Associations between prenatal exposure to both glucocorticoids – particularly cortisol – and tobacco smoke emerged only for daughters, which Stroud says it consistent with some recent research findings.

"Our findings highlight the particular vulnerability of daughters to long-term adverse outcomes following maternal stress and smoking during pregnancy," she said. "We don't yet know why this is, but possible mechanisms include sex differences in stress hormone regulation in the placenta and adaptation to prenatal environmental exposures. Also, cortisol and nicotine may affect developing male and female brains differently."

"Furthermore, if daughters of smoking mothers are more likely to grow up nicotine dependent, the result is dangerous cycle of intergenerational transmission of nicotine addiction," she added.

Despite the warnings and known health risks, approximately one in five expectant moms in the United States continue to smoke during pregnancy. Studies have consistently found that prenatal cigarette smoke exposure is associated with increased rates of behavior problems, irritability, attention-deficit and hyperactivity disorder, the risk of violent offenses, conduct disorder, adolescent onset of drug dependence and the risk for criminal arrest in offspring. This study adds another potential negative outcome – nicotine dependence – to the list of reasons for mothers to stop smoking while pregnant.
Stroud and colleagues studied 1,086 pairs of mothers and their adult children (59 percent female) from the New England Family Study, a 40-year longitudinal follow-up of the Collaborative Perinatal Project based at Brown University. Maternal smoking during pregnancy was assessed prospectively at each prenatal visit, and the mother's cortisol, testosterone and cotinine (a nicotine metabolite passed from mother to infant) levels were measured during the third trimester. The adult children's lifetime nicotine dependence was assessed during a structured interview; the average age at this follow-up was 39.

By studying both maternal smoking and cortisol levels as independent factors, researchers were able to observe whether these two pathways contributed to nicotine dependence in the adult children. They found increased exposure to prenatal glucocorticoids was associated with a 13 percent increased risk of nicotine dependence in daughters only over the 40-year follow-up. Mothers who smoked 15 cigarettes a day or more during pregnancy were 52 percent more likely to have a daughter addicted to nicotine.

"Cigarette smoking is the number one cause of preventable disease, illness and premature death worldwide," said Stroud. "Eliminating smoking during pregnancy and improving the environmental conditions of poor pregnant mothers continues to be a vital challenge for both clinicians and the public health community."

She adds that the findings highlight both the need for enhanced strategies for smoking cessation during pregnancy along with the possibility of targeted smoking cessation efforts later in life, where more intense efforts may be warranted for those with a history of family smoking including prenatal exposure.

**More information:** The report, titled "Prenatal Glucocorticoids and Maternal Smoking During Pregnancy Independently Program Adult Nicotine Dependence in Daughters: A 40-Year Prospective Study," was published online on September 10, 2013.