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Study reveals genetics impact risk of early menopause among some female smokers

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New research is lighting up yet another reason for women to quit smoking. In a study published online in the journal *Menopause*, researchers from the Perelman School of Medicine at the University of Pennsylvania report the first evidence showing that smoking causes earlier signs of menopause – in the case of heavy smokers, up to nine years earlier than average – in white women with certain genetic variations.

Though previous studies have shown that smoking hastens menopause by approximately one to two years regardless of race or genetic background, this study is the first of its kind to demonstrate that genetic background is significantly associated with a further increased risk of menopause in some white women who smoke. No statistically significant relationships between smoking, the gene variants under investigation and earlier menopause were observed in African American women.

While symptoms of menopause – such as hot flashes, anxiety and insomnia – can result in discomfort, embarrassment, and irritability, the onset of menopause is also associated with risks of coronary artery disease, osteoporosis, and death from all causes. On average, women enter menopause at around 50 years of age. However, the research team now reports that menopause may begin at an earlier age in white female smokers who are carriers of two different gene variants. While the genes themselves do not result in early onset menopause, variations of the genes – CYP3A4*1B and CYP1B1*3 – were found to increase the risk of entering menopause at an earlier age in white smokers. The genetic

variants were present in seven and 62 percent of white women in the study population, respectively.

"This study could shed new light on how we think about the reproductive risks of smoking in women. We already know that smoking causes early menopause in women of all races, but these new results show that if you are a white smoker with these specific genetic variants, your risk of entering menopause at any given time increases dramatically," said the study's lead author Samantha F. Butts, MD, MSCE, assistant professor of Obstetrics and Gynecology at Penn Medicine.

Results of the study, which enrolled over 400 women aged 35 to 47 from the Penn Ovarian Aging Study, found that in carriers of the CYP3A4*1B variation, the average time-to-menopause after entering the study in heavy smokers, light smokers, and nonsmokers was 5.09 years, 11.36 years, and 13.91 years, respectively. This means that for heavily smoking white females with this genetic background, the average time-to-menopause was approximately nine years earlier than in nonsmoking carriers.

In white carriers of the CYP1B1*3 variation, the average time-to-menopause in heavy smokers, light smokers, and nonsmokers was 10.41 years, 10.42 years, and 11.08 years, respectively—a statistically significant difference although not as stark as the findings for the CYP3A4*1B variant.

The Penn study did not examine why no statistically significant relationships between smoking, the gene variants under investigation, and earlier menopause were observed in African Americans.

"It is possible that uniform relationships among white and African American women were not found due to other factors associated with race that modify the interaction between smoking and genes," said Butts.

"It is well known that race affects multiple features of menopause, and this could be another. Further investigation is needed to clarify this question."

Provided by University of Pennsylvania School of Medicine