

# Birth control has long-term effect on hormone exposure

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Researchers at Wake Forest University School of Medicine may be one step closer to understanding why past oral contraceptive use dramatically lowers the risk of ovarian and uterine cancers later in life.

While studying the effect of post-menopausal dietary soy consumption on estrogen metabolism in cynomolgus monkeys, Latanya M. Scott, Ph.D., discovered that monkeys who had been given birth control earlier in life had a reduced amount of estrogen excreted in their urine. The research was done in collaboration with Xia Xu, Ph.D., and Timothy Veenstra, Ph.D. at Science Applications International Corporation-Frederick, Inc., in Frederick, Md., who have developed novel methods for analysis of urinary estrogens.

The discovery was particularly noteworthy because it was found three years after oral contraceptive treatment was stopped, roughly the equivalent of a decade of life in a human.

While researchers have known for many years that past oral contraceptive use significantly lowers the risk of ovarian and uterine cancers later in life, this new observation in monkeys may shed light on the mechanism behind the cancer-protective effect of the treatment. Past oral contraceptive use appears to result in a long-term change in the way the monkeys' bodies process hormones. While researchers don't yet understand the precise mechanism by which hormone levels are being affected, they do know that both the level of estrogen in the blood and the amount of estrogen being excreted in urine are lowered with past oral

contraceptive use, which may mean that the oral contraceptive use is somehow leading to a diminished synthesis of estrogen.

The study appears in this month's issue of *Cancer Epidemiology, Biomarkers and Prevention*.

"Hormone exposure has long been known to be important in cancer risk," said J. Mark Cline, D.V.M., Ph.D., and senior researcher on the project. "These effects are robust, and we believe this discovery could be translated fairly quickly into a study in women. If our results are confirmed to also occur in women, they could change the way we look at oral contraceptives and cancer risk," added Cline, a professor of pathology and comparative medicine.

With funding from the National Institutes of Health, researchers began with 181 premenopausal cynomolgus monkeys and followed them for seven years in a study designed to look at hormone effects on many aspects of female health.

Half of the monkeys were given a birth control treatment of triphasic estrogen and progestin, marketed by Wyeth Pharmaceuticals as Triphasil™, for 26 months. At the end of the premenopausal phase of the study, the animals underwent surgery to have their ovaries removed, making them surgically menopausal.

The postmenopausal monkeys were then divided into three dietary intervention groups to evaluate the effects of soy on hormone metabolism.

Urine samples were collected from each monkey during the 35th and 36th months of the postmenopausal phase of the study and frozen for subsequent analysis of metabolite concentrations.

Lab results showed that the premenopausal use of oral contraceptives resulted in significantly lower levels of most estrogen metabolites three years after surgical menopause. Among the most abundant metabolites, percent changes ranged from a 25 percent reduction in E1 to a 50 percent reduction in 2OHE1 with oral contraceptive administration. Postmenopausal dietary isoflavones induced fewer significant effects on postmenopausal estrogen metabolite concentrations.

"The magnitude and persistence of oral contraceptive effect really surprised us," said Cline, a diplomate of the American College of Veterinary Pathologists. "It tells us that there may be a new and potentially strong cancer-protective mechanism at work. This could open new doors of inquiry in the field."

Source: Wake Forest University

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