Pregnancy problems may lead to later cardiac trouble in adult children

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A new study in *Cardiovascular Research* finds that female offspring of females with polycystic ovary syndrome have an increased risk for developing cardiac dysfunction.

Polycystic ovary syndrome is the most common reproductive disorder, affecting one in 10 women of childbearing age. Women with disorder may have infrequent or prolonged menstrual periods or excess male hormone (androgen) levels, making pregnancy more difficult. The disorder is also associated with developing type 2 diabetes, depression, high blood pressure, and uterine cancer.

Although the disorder has a strong genetic component, considerable evidence suggests that the syndrome may originate by an adverse environment in utero with maternal androgen excess.

Researchers here tested the hypothesis that elevated maternal dihydrotestosterone during late pregnancy may cause cardiac dysfunction in adult female offspring.

Researchers conducted three experiments to assess the effects of prenatal exposure to dihydrotestosterone, as well as maternal obesity, in mice. Researchers generated prenatally androgenized female offspring by injecting pregnant dams with dihydrotestosterone during late pregnancy. To generate maternal obesity, twelve-week-old female mice were fed for 10 weeks with a high-fat/high-sucrose diet prior to and during pregnancy. After birth, female offspring were separated from their mothers and assigned to a control diet. The cardiac function was measured with echocardiography in a subset of adult female mice offspring and the heart tissue was thereafter harvested for molecular analysis.

Researchers also measured the effects of continuous dihydrotestosterone exposure from pre-puberty to adult age in cardiac function, using a mouse model that resembles features of the human polycystic ovary condition. In this experiment, 4-week-old female mice were implanted subcutaneously with either an implant containing dihydrotestosterone; or an empty, blank implant; or a pellet containing flutamide (an anti-androgen) together with the dihydrotestosterone -containing pellet. Seven weeks after pellet implantation, mice were subject to cardiovascular assessment.

Throughout the experiments, researchers found that maternal androgen excess as well as continuous androgen exposure from pre-puberty leads to pathological cardiac hypertrophy in adult life. Moreover, they showed that the cardiac dysfunction in the adult prenatally androgenized offspring was linked to an early cardiac reprogramming. Maternal high-fat/high sucrose feeding prior to and during gestation alone did not have an impact on the cardiac profile of the female offspring.

"Our study provides novel insight into the mechanisms that may lead to increased risk of developing cardiovascular disease in women with PCOS and their daughters. We revealed that exposure to male hormones during the critical period of fetal life is a stronger factor than maternal obesity in PCOS, which has a long-lasting impact on the cardiovascular profile of female offspring", says Stener-Victorin.

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