

Smoking and pre-eclampsia may cause fertility problems for offspring, study suggests

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Low levels of oxygen in the womb—which can be caused by smoking or conditions such as pre-eclampsia—may cause problems with fertility

later in life, a study carried out in rats suggests.

The research, led by scientists at the University of Cambridge, found that exposing fetuses to chronic [hypoxia](#) (low oxygen levels) during development led to them having advanced ageing of the ovaries and fewer eggs available.

Hypoxia in the womb can be caused by a number of factors, including smoking, pre-eclampsia, maternal obesity, and living at high altitude. The condition is already known to have potential long term effects on the health of offspring, including increased risk of heart disease. However, this study, published today in *The FASEB Journal*, is the first time it has been shown to affect fertility.

To investigate the effects of hypoxia, researchers from the Metabolic Research Laboratories at the University of Cambridge placed pregnant female rats in reduced levels of oxygen (13%, compared to the standard 21% found in air) from day six to day 20 of their [pregnancy](#). They then examined the reproductive tract of their female pups at age four months.

Rats are a useful model for studying pregnancy. As a mammal, their bodies and underlying biology share some key similarities with those of humans. However, their gestation period and lifecycles are much shorter than those of humans, making them an ideal animal model in which to study pregnancy and [fetal development](#).

When the team examined the pups, they found a decrease in the number of ovarian follicles in the reproductive tract. Females are born with fixed numbers of follicles, each with the potential of developing into an egg. In humans, [women](#) usually expend all their eggs around the age of fifty, at which point they will enter menopause.

The researchers also looked at telomere length in the pups' [ovarian tissue](#)

. Telomeres are found at the end of chromosomes and prevent the chromosome from deteriorating—they are often compared to the plastic that seals the end of shoe laces. As we age, telomeres become shorter and shorter, and hence their length can be used as a proxy to measure ageing. The researchers found that telomeres in the ovarian tissue of pups exposed to hypoxia were shorter than in unexposed pups.

"It's as if low levels of oxygen caused the female's ovarian tissue to age faster," says Dr. Catherine Aiken from the University of Cambridge. "Biologically, the tissue appears older and the female would run out of eggs—in other words, become infertile—at a younger age."

Although the research was carried out in rats, Dr. Aiken says there is every reason to expect that the findings could be translated to humans as previous studies looking at hypoxia during pregnancy in relation to other conditions such as heart disease have been shown to be relevant in humans.

While women are recommended not to smoke during pregnancy, other causes of hypoxia, such as pre-eclampsia and living in a high altitude, are beyond their control. However, says Dr. Aiken, the findings of her team's research may prove helpful to women who were exposed to low levels of oxygen during their mother's pregnancy.

"Now that we've seen a link between hypoxia and fertility problems in rats, we know what to look for in women," she says. "If the same turns out to be true for them, then women at risk will be able to take action: by having children earlier in life or looking to assisted reproduction, such as IVF, there should be no reason why these women cannot have children."

Dr. Aiken is also involved in research looking at whether anti-oxidant medication may help undo any damage caused by hypoxia.

More information: Catherine E. Aiken et al, Chronic gestational hypoxia accelerates ovarian aging and lowers ovarian reserve in next-generation adult rats, *The FASEB Journal* (2019). [DOI: 10.1096/fj.201802772R](https://doi.org/10.1096/fj.201802772R)

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