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Painkillers in pregnancy may affect baby's future fertility

Taking painkillers during pregnancy could affect the fertility of the unborn child in later life, research suggests.

The study identifies that these drugs may also affect the fertility of future generations, by leaving marks on DNA.

The findings add to a growing body of evidence that certain medicines, including paracetamol, should be used with caution during pregnancy.

Researchers stress that advice for pregnant women remains unchanged. Current guidelines say that, if necessary, paracetamol – also known as acetaminophen – should be used at the lowest possible dose for the shortest possible time. Ibuprofen should be avoided during pregnancy.

Scientists at the University of Edinburgh looked at the effects of paracetamol and ibuprofen on samples of human fetal testes and ovaries. They found similar effects using several different experimental approaches, including lab tests on human tissue samples and animal studies.

Human tissues exposed to either drug for one week in a dish had reduced numbers of cells that give rise to sperm and eggs, called germ cells, the study found.

Ovaries exposed to paracetamol for one week had more than 40 per cent fewer egg-producing cells. After ibuprofen exposure, the number of cells was almost halved.

Experts say this is important because girls produce all of their eggs in the womb, so if they are born with a reduced number it could lead to an early menopause.

Painkiller exposure during development could have effects on unborn boys too, the study found. Testicular tissue exposed to painkillers in a culture dish had around a quarter fewer sperm-producing cells after exposure to paracetamol or ibuprofen.

The team also tested the effects of painkiller treatment on mice that carried grafts of human fetal testicular tissue.

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These grafts have been shown to mimic how the testes grow and function during development in the womb.

After just one day of treatment with a human-equivalent dose of paracetamol, the number of sperm-producing cells in the graft tissue had dropped by 17 per cent. After a week of drug treatment, there were almost one third fewer cells.

Previous studies with rats have shown that painkillers administered in pregnancy led to a reduction in germ cells in female offspring. This affected their fertility and the fertility of females in subsequent generations.

The scientists found that exposure to paracetamol or ibuprofen triggers mechanisms in the cell that make changes in the structure of DNA, called epigenetic marks. These marks can be inherited, helping to explain how the effects of painkillers on fertility may be passed on to future generations.

Painkillers' effects on germ cells are likely caused by their actions on molecules called prostaglandins, which have key functions in the ovaries and testes, the researchers found.

The study, published in *Environmental Health Perspectives*, was funded by the Medical Research Council, Wellcome and the British Society of Paediatric Endocrinology and Diabetes.

Dr Rod Mitchell, who led the research at the University of Edinburgh's MRC Centre for Reproductive Health, said: "We would encourage women to think carefully before taking painkillers in pregnancy and to follow existing guidelines – taking the lowest possible dose for the shortest time possible."

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Journal article:

P. Hurtado-Gonzalez et al. Effects of Exposure to Acetaminophen and Ibuprofen on Fetal Germ Cell Development in Both Sexes in Rodent and Human Using Multiple Experimental Systems. *Environmental Health Perspectives*, 2018.

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Advance copies of the paper are available from jen.middleton@ed.ac.uk.

Once published, the paper will be available online from <https://ehp.niehs.nih.gov/ehp2307>

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