With worrisome animal research, more focus needed on effects of cannabis on human development

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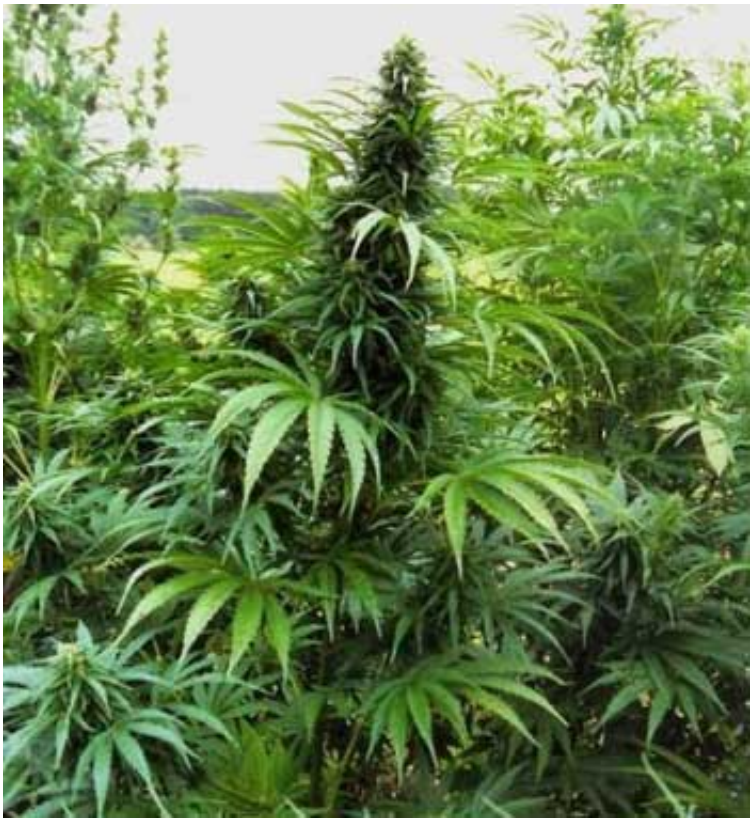

Cannabis indica. Credit: Wikipedia

In this new era of legalized marijuana, far too little research has been conducted on the effect of cannabis on the development of human embryos, say researchers at Georgetown University Medical Center who

scoured medical literature on the topic and found what they say is worrisome animal research.

Their study, in the journal *BioMed Central* (*BMC*) *Pharmacology and Toxicology*, suggests an urgent need for human epidemiological and basic research that examines the link between maternal cannabinoid use, either smoked or eaten in candy bars, and the health of newborns. Cannabinoids are chemicals like THC, the primary psychoactive compound in marijuana, that act on cannabinoid receptors in neurons, repressing the normal release of neurotransmitters.

"We know from limited human studies that use of marijuana in early pregnancy is associated with many of the same risks as tobacco, including miscarriage, birth defects, developmental delays and learning disabilities, but animal research suggests the potential for many more developmental issues linked with the drug," says the study's senior investigator, G. Ian Gallicano, PhD, associate professor of biochemistry and molecular & cellular biology at Georgetown.

Gallicano says one reason for limited research is that the classification of marijuana as a Schedule I drug creates challenges to conducting research.

"All of the model systems point to the notion that cannabinoids affects many aspects of human development because THC and other chemicals alter molecular pathways that shouldn't be disrupted during development of a fetus," he says.

"We also know that THC is a promising agent for treating cancer, because it negatively affects tumor growth and can cause the death of cancer cells. Embryo development has similarities to tumor formation—it turns on growth pathways that are necessary for development," Gallicano says. "The fact that THC seems to stop cancer

growth suggests how damaging the chemical could be for a fetus."

The study grew from a project of four current Georgetown medical students (Joseph Friedrich, Dara Khatib, Keon Parsa, and Ariana Santopietro) for a course, Sexual Development and Reproduction, taught by Gallicano. They undertook the analysis given that although four states have legal recreational marijuana use and 24 allow use of medical marijuana, little research has been conducted on outcomes from use of the drug in pregnancy and biological mechanisms that cause these issues.

The students reviewed the scientific literature for studies on cannabinoids and embryonic development published between 1975 and 2015. They cite the following findings:

- THC lasts in the body for weeks, especially in maternal tissues that act as reservoirs for THC and other cannabinoids, according to studies of pregnant dogs. Human cells studies have shown that THC has a half-life of eight days in fat deposits and can be detected in blood for up to 30 days;
- THC readily crosses the human placenta, which can slow clearance of the drugs while prolonging fetal exposure;
- THC levels in smoked marijuana have increased nearly 25-fold since 1970, and can be substantially stronger in edible preparations of cannabis;
- THC and other cannabinoids interfere with use of folic acid (vitamin B9), which has long been known to be essential for normal development and growth of the human placenta and embryo. Deficiencies in folic acid are linked to low human birth weight, increased risk of spontaneous abortion, and neural tube defects such as spina bifida.
- Cannabinoid signaling plays important roles in development of a mouse embryo. It is required for proper pre-implantation development, embryo transport to the uterus, and implantation.

- In post-implantation development, cannabinoid signaling functions in a multitude of pathways, including, but not limited to blood vessel growth, fate of embryonic stem cells, and normal cognitive development. For example, disruption of one key neural pathway, BDNF, has been linked to increased risk of congenital malformations and impaired cognition, including autism and low IQ in humans.

The authors also say the harms found in animal studies cited in this study do not include the damaged induced from the act of smoking marijuana.

Provided by Georgetown University Medical Center

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