New study shows paternal alcohol use increases frequency of fetal development issues

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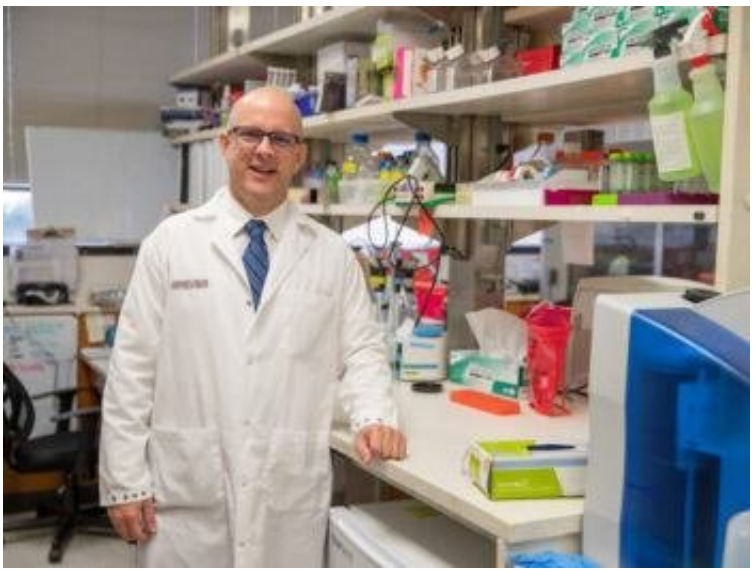

Michael Golding, associate professor in Texas A&M's Department of Veterinary Physiology & Pharmacology. Credit: Texas A&M College of Veterinary Medicine & Biomedical Sciences

Prenatal visits have traditionally focused almost exclusively on the behavior of mothers, but new research from the Texas A&M College of Veterinary Medicine & Biomedical Sciences (CVMBS) continues to suggest that science should be looking more closely at the fathers' behavior as well.

Dr. Michael Golding, an associate professor in the CVMBS' Department of Veterinary Physiology & Pharmacology (VTPP), has spent years investigating the father's role, specifically as it relates to drugs and alcohol, in fetal development.

Golding says a number of publications have shown that males pass down more than just their genetics, but exactly how that process works and the consequences of it remain largely unknown.

"When you look at the data from throughout human history, there's clear evidence that there's something beyond just genetics being inherited from the male," Golding said. "So, if that data is solid, we've got to start looking more at male behavior.

"Say you had a parent who was exposed to starvation—they could pass on what you might call a 'thriftiness,' where their kids can derive more nutrition from less food," he said. "That could be a positive if they grow up in a similar environment, or they could grow up in a time when starvation isn't an issue and they might be more prone to obesity or metabolic syndromes. That kind of data is clearly present in clinical data from humans."

Golding's study of how things beyond genes, such as behavior and environment, affect development is called epigenetics, and one of the big questions in the search for answers on how male prenatal behavior can impact fetal growth has been how exactly these epigenetic factors manifest.

Now, there is at least one answer.

In a November publication in the *FASEB Journal*, Golding's team showed that the epigenetic factor of prenatal exposure to alcohol in males can manifest in the placenta.

According to Kara Thomas, VTPP graduate student and the lead author on the paper, their data shows that in mice, offspring of fathers exposed to alcohol have a number of placenta-related difficulties, including increased fetal growth restriction, enlarged placentas, and decreased placental efficiency.

"The placenta supplies nutrients to the growing fetus, so fetal growth restriction can be attributed to a less efficient placenta. This is why placental efficiency is such an important metric; it tells us how many grams of fetus are produced per gram of placenta," Thomas said. "With paternal alcohol exposure, placentas become overgrown as they try to compensate for their inefficiency in delivering nutrients to the fetus."

However, the mystery also deepened.

While these increases happened frequently in male offspring, the frequency varied greatly based on the mom; however, the same increases were far less frequent in female offspring. Golding believes this suggests that although that information is passed from the father, the mother's genetics and the offspring's sex also play a role.

"This is a novel observation because it says that there's some complexity here," Golding said. "Yes, men can pass things on to their offspring beyond just genetics, but the mom's genetics can interpret those epigenetic factors differently, and that ultimately changes the way that the placenta behaves."

These results don't draw a clear line in how human male drinking prior to conception impacts fetal development, but they continue to at least point to it being a question that needs to be explored.

Golding is hoping that soon doctors, and society at large, will begin to ask more questions about male prenatal behavior so that there's more

data from which to work.

"The thing that I want to ultimately change is this stigma surrounding the development of birth defects," Golding said. "There's information coming through in sperm that is going to impact the offspring but is not tied to the genetic code; it's in your epigenetic code, and this is highly susceptible to environmental exposures, so the birth defects that we see might not be the mother's fault; they might be the father's or both, equally."

More information: Kara N. Thomas et al, Maternal background alters the penetrance of growth phenotypes and sex-specific placental adaptation of offspring sired by alcohol-exposed males, *The FASEB Journal* (2021). DOI: 10.1096/fj.202101131R

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