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New sheep obesity research that could affect future generations

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Stephen Ford, the University of Wyoming's Rochelle Endowed Chair in the Department of Animal Science, takes a blood sample from a pregnant ewe. Ford is lead writer of a paper that was recently published in the International Journal of Obesity. Credit: Megan Walton

Obesity in female sheep during pregnancy can impact the metabolic profile and health of the animals' granddaughters, as well as their daughters, suggests a study published in the *International Journal of Obesity* Oct. 30.

The study has implications for predicting obesity, particularly abdominal fat, in humans.

Stephen Ford, the University of Wyoming's Rochelle Endowed Chair in the Department of Animal Science and director of the Center for the Study of Fetal Programming, is lead writer of a paper, titled "Multi-Generational Impact of Maternal Over-nutrition/Obesity in the Sheep on the Neonatal Leptin Surge in Granddaughters." *The International Journal of Obesity* provides an international, multi-disciplinary forum for the study of obesity. The journal publishes basic, clinical and applied studies and also features a quarterly pediatric highlight.

The multigenerational effects of over-nutrition during pregnancy on body-fat levels, and blood glucose and insulin concentrations, have been studied in rodents, but it remains uncertain whether the same findings apply to large-animal species, including humans, that tend to bear a single fetus born after a greater degree of intra-uterine development.

Ford's research makes those previously unknown factors more quantifiable.

"The most interesting thing is this is the first paper that looks at large mammals that gives attention in the phenotype or change in their propensity to get fat," Ford says. "This has been shown in rodents."

Ford and colleagues compared 20 obese, over-nourished ewes with a control group of 20 ewes that were fed only to requirements. They examined how obesity and overfeeding affected the animals' daughters (referred to as F1s) and granddaughters (known as F2s). The authors found that birth weight did not vary significantly between granddaughters of the two treatment groups.

However, newborn lambs born to the daughters of over-nourished pregnant sheep (those that reached 70 percent to 80 percent beyond their normal weight) had higher adiposity or obesity levels, and higher blood concentrations of glucose and insulin, compared to granddaughters of the

control group.

In several mammalian species, including sheep, there is a surge of leptin—a hormone involved in regulating appetite by organizing the brain structures that control our appetite—during the first two to three weeks of postnatal life, which can be altered by diet-induced obesity. This alteration occurs when leptin surge does not occur in the newborn during the first few weeks after birth. As a result, the sheep is predisposed to having weight struggles because the mother was overweight during pregnancy, Ford says.

In this study, Ford and co-writers found that there was a lower leptin peak in granddaughters of over-nourished sheep than in granddaughters of the control group. This may make granddaughters of over-nourished sheep more susceptible to increased appetite, obesity, and insulin and leptin resistance in adulthood. The granddaughter sheep, or F1 offspring, were studied until they were 2 years of age, which is considered adulthood for the sheep, Ford says.

Human relativity

Ford says his study of sheep could easily correlate to humans and their struggles with controlling weight.

"That's bad news for humans. If a mother took care of herself during pregnancy, the granddaughter has some propensity or some chance of becoming obese when she develops," Ford says. "Sheep are a lot like us. They have no satiety center. They don't know when to stop eating."

A sheep's pregnancy period is roughly 150 days compared to a human's average of 275 days.

Of pregnant women in the U.S., 18 percent to 35 percent are estimated

to be clinically obese, according to a book, titled "Prevalence and Trends in Obesity Among U.S. Adults, 1999-2008" (2010).

In the U.S., it is estimated that 68 percent of the population is overweight, and that 33.3 percent of men and 35.3 percent of women are obese, according to the previously referenced book.

The National Institutes of Health (NIH) reports that 30 percent of women of child-bearing age are overweight or obese at conception and remain so throughout pregnancy. Maternal obesity not only predisposes mothers to serious health problems during pregnancy, but also increases the incidence of chronic metabolic diseases in their children and grandchildren. These include hyperphagia (overeating), insulin resistance, obesity, type 2 diabetes, hypertension and cardiovascular disease.

The paper's writers note that further research is needed to fully understand the processes that govern these multigenerational effects and to explore whether and to what extent epigenetic mechanisms (whereby environmental factors program changes in gene expression) are involved.

Peter Nathanielsz, co-director of UW's Center for the Study of Fetal Programming; John Odihiambo, a current UW post-doctoral researcher from Homa Bay, Kenya; Nathan Long, a former UW post-doctoral researcher and now an assistant professor in Clemson University's Department of Animal and Veterinary Sciences; Nuermaimaiti Tuersunjiang, a former UW doctoral student and now a post-doctoral scientist at the Texas Biomedical Research Institute in San Antonio; and Desiree Sasha, a UW master's student from Rockaway, N.J., majoring in animal science, contributed to the paper.

More information: "Multi-generational impact of maternal overnutrition/obesity in the sheep on the neonatal leptin surge in

granddaughters." *International Journal of Obesity* (30 October 2014) | DOI: 10.1038/ijo.2014.190

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