

Lambs provide crucial link in understanding obesity

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The research, published today in *The Journal of Physiology*, shows a definite link between maternal and offspring obesity and is the first demonstration that this is the case in mammals which bear 'mature offspring' – as humans do.

Professor Peter Nathanielsz, lead author of the research, said: "A relationship between maternal <u>obesity</u> and offspring obesity has been clearly identified in rodents but as their young are born immature, it was not clear whether the findings would apply to humans.

"Lambs offer a more similar model to understand the mechanism of human obesity as they are born at a more advanced level of maturity – equivalent to humans."

For 60 days before conception and throughout their pregnancy Nathanielsz and his team at the Center for Pregnancy and Newborn Research, University of Texas and the University of Wyoming, fed sheep either a normal diet or one that produces obesity. The appetite and weight gain of their offspring were then monitored for a further 19 months.

By taking frequent blood samples from the newborn lambs, the team were able to monitor levels of hormones that are known to affect developmental programming – in particular the hormone leptin. Leptin is produced by adipose fat cells and regulates appetite. In lambs born of normal weight mothers, there was a peak in leptin in the sixth to ninth



days of life but this peak did not occur in lambs born to obese ewes.

"The neonatal peak in leptin plays a central role in the development of areas of the brain that regulate appetite. We have found that an absence of this peak in lambs born to obese mothers seems to predispose them to increased appetite and obesity in later life."

Blood samples taken from one day old lambs also found that cortisol levels were up to 50% higher in obese sheep, leading the team to suspect that exposure to higher levels of cortisol in the womb may prevent the normal leptin rise in lambs of obese mothers.

"We propose that cortisol prepares fetal adipose tissue to secrete leptin – and that this process seems to be disrupted in lambs born to obese mothers. The nutrient excess present in the blood of obese mothers throughout gestation seems to inhibit the post-natal leptin peak – which likely has important consequences for the development of the lamb."

"Given the epidemic of obesity both in the developed and developing world, the search for environmental factors occurring around the time of birth which predispose <u>offspring</u> of overweight mothers to lifelong obesity is important.

"Seeing these hormonal change in lambs, in addition to what we have already found with rodents, is advancing our understanding of what programmes appetite. We are getting closer to understanding what causes obesity in humans." concluded Nathanielsz.

Provided by Wiley

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