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**The effects of uterine environment upon embryonic,  
fetal, neonatal and post-natal development and  
glucose metabolism in sheep**

A thesis presented in partial fulfilment of the requirements  
for the degree of Doctor of Philosophy  
in Veterinary Science at Massey University,  
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## Abstract

Studies of humans and domestic animals have shown that there is a linkage between the neonatal and post-natal health of an individual and its uterine environment during gestation. However, very little information exists for sheep and there have been no studies that have directly examined the stage of gestation at which such effects could be introduced to the conceptus.

In the present study, pure-breed embryos were transferred within and reciprocally between large (Suffolk: S) and small (Cheviot: C) breeds of sheep to establish different uterine environments; SinS (large control), SinC (restricted environment), CinS (luxurious environment) and CinC (small control) and their effects upon embryonic, fetal, neonatal and post-natal development and glucose metabolism of lambs were examined.

By Day 19 of gestation, conceptuses (embryo and trophoblast) developing in a restricted uterine environment (SinC) were smaller ( $P < 0.05$ ) than in control (SinS). The head length of SinC fetuses was smaller ( $P < 0.05$ ) than in SinS fetuses on Day 55 of gestation and SinC lambs were lighter and smaller ( $P < 0.05$ ) than SinS lambs at birth. During subsequent post-natal life, there was no difference ( $P > 0.05$ ) in the growth rate of SinC and SinS lambs. The liveweight and body dimensions of SinC lambs were lower ( $P < 0.05$ ) than SinS lambs until 9 weeks and 12 weeks of age, respectively. Day 19 peri-implantation embryos and trophoblasts that developed in a luxurious environment were bigger than in control (CinC). However, CinS fetal size did not differ ( $P > 0.05$ ) from CinC fetuses by Day 55 of gestation. There was no difference ( $P > 0.05$ ) in the birthweight and body dimensions of lambs born from these two groups. Dimension of the placentas of SinC and SinS or CinS and CinC

did not differ ( $P < 0.05$ ) during gestation or at lambing. Concentrations of ovine placental lactogen (oPL), progesterone, insulin-like growth factor-1 (IGF-1), glucose and free fatty acid (FFA) differed between uterine environments. During glucose challenge tests, there were no differences in the concentrations of glucose and insulin, between SinC and SinS female lambs, however, glucose concentrations declined more rapidly ( $P < 0.05$ ) in CinS than CinC female lambs at one year of age.

It was concluded that restricted uterine environment affects embryonic, fetal and neonatal development of lambs, and that these effects perpetuates until at least one year of age; but there was no effect upon glucose metabolism. Conversely, a luxurious uterine environment enhances the early development of embryos but had no effects upon subsequent fetal, neonatal and post-natal development; however glucose metabolism of post-natal female lambs was improved. It appears that these effects of uterine environment were mediated through the trophoblast during the early embryonic period and via the placenta during subsequent gestation. oPL, progesterone, IGF-1, glucose and FFA were implicated in feto-maternal dialogue. These results suggest that uterine environment significantly influences the biology of young sheep with possible economic consequences.

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## List of Abbreviations

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AUC	area under curve
BNC	binucleate cells
CIDR	controlled internal drug release
cm	centimetre
cpm	counts per minute
DNA	deoxyribo nucleic acid
FFA	free fatty acid
g	gram(s)
GLUT1	glucose transporter 1
GLUT3	glucose transporter 3
GLUT4	glucose transporter 4
h	hour(s)
IGFs	Insulin-like growth factors
IGF-1	Insulin-like growth factor-1
IGF-1R	Insulin-like growth factor receptor-1
IGF-2	Insulin-like growth factor-2
IGF-2R	Insulin-like growth factor receptor-2
IGFBP	Insulin-like growth factor binding protein
IU	international unit(s)
kDa	kilo Dalton
kg	kilogram(s)
L	litre
LA	long acting
µg/dL	micrograms per decilitre
µIU/L	micro international unit(s) per litre
µIU/mL	micro international units per millilitre
µL	microlitre
µm	micrometre
mg	milligram(s)
min	minute(s)
min µIU/L	minute micro international unit(s) per litre
min mmol/L	minute milli mol per litre
mL	millilitre
mm	millimetre(s)
mmol/L	milli mol per litre
mRNA	messenger ribonucleic acid
n	number
ng/dL	nanograms per decilitre
NIH	National Institute of Health
oPL	ovine placental lactogen
PAS	Periodic Acid Schiff's

RIA	radio-immuno assay
rpm	revolutions per minute
SD	standard deviation
SE	standard error
VHS	video home system
vs	versus
wt	weight
$\Pi$	pi
%	percent
$^{125}\text{I}$	$^{125}$ Iodine
$^{\circ}\text{C}$	degree(s) celsius

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