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Protein restriction during early gestation impairs renal function in sheep with adult-onset obesity

Clint Gray[1], Phillip Rhodes[1], Stuart Rhind[2] and David Gardner[1]
[1]*School of Veterinary Medicine & Science, University of Nottingham, Sutton Bonington, UK and* [2]*Macaulay Research Institute, Craigiebuckler, UK*

There is much evidence from animal studies that the fetal environment encountered during critical stages of gestation may alter the developmental pathway of the fetus[(1)]. Prenatal nutritional restriction affects the delicate balance of biochemical pathways that ensure optimal development of tissues and organs. These maladaptations *in utero* have been shown to be associated with adult-onset pathophysiology such as glomerulosclerosis and hypertension; combined, these conditions often lead to end-stage renal disease (ESRD)[(2)].

In the present unique study pregnant sheep were fed a low-protein diet during early or late gestation and the resulting offspring followed to 2 years of age, when *in vivo* renal function was assessed using renography.

Nineteen pregnant Scottish Blackface sheep were either fed a diet that met their protein and energy requirements from day 0 (mating date) to term (approximately 145 d gestation; CP; *n* 7) or a diet low in protein (g protein/kg; 90 *v.* 180) during early (0–65 d gestation; LPE; *n* 6) or late (65 d gestation to term; LPL; *n* 6) gestation. Lambs were delivered naturally and were ewe-reared to weaning at 10 weeks and then fed grass until 1.5 years of age. At this time, all lambs were barn housed to restrict physical activity and offered a diet higher in fat (60 g palm kernel oil/kg) at 1.5 × maintenance to encourage weight gain. Renal function was assessed by gamma scintigraphy using Tc (Tc^{99}-labelled DTPA). Briefly, 100 MBq was injected intravenously and the passage of the radionuclide through each kidney followed for 20 min, in a total of sixty frames. Calculated variables included time to peak (min) and up slope (counts per min; cpm), which indicate rate of uptake into the kidneys, and down slope (cpm) and transit time (min), which show clearance and excretion by the kidneys. Data are presented as estimated marginal means generated by the univariate general linear model procedure in SPSS version 14 (SPSS Inc., Chicago, IL, USA), with treatment (CP *v.* LPE *v.* LPL), gender (male or female) and sibling (single or twin) as fixed effects. Significance was $P<0.05$.

All sheep became similarly obese as a result of the postnatal dietary treatment (approximately 30% body fat mass, as assessed by dual-energy X-ray absorptiometry).

	CP		LPE		LPL		
	Mean	SE	Mean	SE	Mean	SE	*P* =
Time to peak (min)							
Left kidney	3.0	0.15	3.20	0.04	2.78	0.11	0.03
Right kidney	3.13	0.07	3.07	0.05	2.98	0.12	0.058
Down slope (cpm)							
Left kidney	8.03	0.35	2.6	0.27	5.28	0.26	0.002
Transit time (min)							
Left kidney	1.06	0.06	1.25	0.04	0.93	0.04	0.02
Right kidney	1.10	0.19	1.27	0.07	0.93	0.07	0.067

Prenatal low-protein diets have generally been shown to significantly (>40%), and may permanently, reduce offspring nephron endowment. In sheep, as oppose to rats, nephrogenesis ends *in utero* at about day 120, which is a similar stage to the end of human nephrogenesis at about week 36 (0.9 of gestation). The present study has shown that a low-protein diet during early, but not late, nephrogenesis negatively impacts on offspring renal function, superimposed on prevailing obesity. Radionuclide uptake and clearance was markedly decreased, potentially providing an early *in vivo* and non-invasively-obtained marker for later renal failure. Future work will consider nephron number in these animals and whether early glomerulosclerosis is evident and influenced by prenatal diet.

1. McMillen C & Robinson JS (2005) *Pysiol Rev* **85**, 571–633.
2. Hershkovitz D, Burbea Z, Skorecki K & Brenner BM (2007) *Clin J Am Soc Nephrol* **2**, 334–342.