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Protein restriction *in utero* programmes renal calcium handling and bone morphology in the rat

N. Ashton[1] and A.J. Freemont[2]

[1]School of Biological Sciences, University of Manchester, Manchester, M13 9PT, UK and [2]Academic Unit of Laboratory Medicine, University of Manchester, Manchester, M13 9PT, UK

Exposure to a maternal low protein diet *in utero* programmes the rat foetus to develop hypertension (Langley & Jackson, 1994) and impaired renal function (Sahajpal & Ashton, 2003). Studies on senescent rats also revealed a long term reduction in bone area and bone mineral content, with a widening of the epiphyseal growth plate (Mehta *et al.*, 2002), suggesting that skeletal growth may also be programmed *in utero*. The aim of this study was to determine the effects of a maternal low protein diet on renal calcium handling and bone morphology in young rats.Pregnant Wistar rats were fed isocalorific diets containing either 18% (normal, NP) or 9% (low, LP) protein from conception (Sahajpal & Ashton, 2003). After birth, all dams switched back to standard rat chow. Male offspring (NP n = 5-6 from n = 5 litters, LP n = 5-7 from n = 5 litters) were studied at 4 weeks of age. Renal clearance of ^{3}H inulin and calcium was measured under Intraval anaesthesia (thiopentone sodium, 110 mg kg^{-1}, i.p.) in rats receiving euvolaemic fluid replacement of spontaneous urine output (Ahmed *et al.*, 2003). Animals were humanely killed at the end of the experiment. Femurs were decalcified for histomorphometric assessments of matrix. Statistical comparisons were by unpaired *t*-test. Mean arterial blood pressure was higher (NP, $n = 6, 82 \pm 6$ vs LP, $n = 7, 111 \pm 5$ mmHg, $P<0.01$) and body weight was lower (NP 114.5 ± 3.6 vs LP 90.7 ± 5.2 g, $P<0.01$) in LP rats. Glomerular filtration rate (GFR) was lower, but calcium clearance (C_{Ca}) and both total ($U_{Ca}V$) and fractional excretion (FE_{Ca}) of calcium were higher in LP rats (Table 1).

	NP (n;=6)	*LP (n;=7)*
GFR (ml min^{-1} 100g bwt^{-1})	*1.3±0.1*	*0.9 ±0.1****
C_{Ca} (µl min^{-1} 100g bwt^{-1})	*3.8±0.8*	*12.7±2.1****
$U_{Ca}V$ (µmol min^{-1} 100g bwt^{-1})	*0.01±0.002*	*0.03±0.005***
FE_{Ca} (%)	*0.3±0.06*	*1.49±0.25****

This was associated with significantly lower total plasma calcium concentration (NP, $n = 6, 2.87 \pm 0.21$ vs LP, $n = 7, 2.09 \pm 0.1$ mmol l^{-1} $P<0.01$). Table 1. Glomerular filtration rate and renal handling of calcium by 4 week old NP and LP rats. ** $P<0.01$, *** $P<0.001$Trabecular bone mass in the lower femur was lower in LP rats (NP, $n = 15, 21.6 \pm 4.3$ vs LP, $n = 15, 9.3 \pm 2.1$ %, $P<0.01$). The area of new bone formation at the underside of the growth plate was greater in LP compared with control rats (NP, $n = 15$, 43.0 ± 4.5 vs LP, $n = 15$, 59.9 ± 4.6 %, $P<0.05$).These data show that renal calcium handling is programmed *in utero* which may impact upon bone formation.

Ahmed, M.H., *et al.* (2003). *J Pharmacol Exp Ther* **304**, 156-161.

Langley, S.C. & Jackson, A.A. (1994). *Clin Sci* **86**, 217-222.

Mehta, G., *et al.* (2002). *Calcif Tissue Int* **71**, 493-498.

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Where applicable, the experiments described here conform with Physiological Society ethical requirements.