The effects of maternal renal dysfunction and a high salt diet on the renin angiotensin systems of the pregnant ewe and her fetus

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We previously reported that maternal renal dysfunction, caused by subtotal nephrectomy (STNx) prior to mating, resulted in fetuses with high urine flow rates, high urinary sodium excretions and low haematocrits (Gibson *et al*., 2002). These changes were suggestive of exposure to an increased fluid and solute load from the mother. To determine whether the fetal renin angiotensin system was suppressed, we measured plasma renin levels in 17 STNx and 14 control ewes and their fetuses at 122-128 days gestation (term = 150 days). In addition, we examined the effects of a high salt diet.

At least two months prior to mating, STNx was carried out under general anaesthesia (1 g sodium thiopentone i.v. followed by 1-3% halothane in oxygen). The right kidney was removed and a branch of the left renal artery (supplying at least one third of the kidney) was ligated. At 112-122 days the fetuses and ewes were chronically catheterised under general anaesthesia. No measurements were taken until at least 5 days after surgery. Plasma renin levels were measured as the rate of generation of angiotensin I (ng ml^{-1} h^{-1}) in samples incubated with nephrectomised sheep plasma (a source of angiotensinogen).

Maternal renin levels were similar in the two groups (Control 1.4 ± 0.4 (SE), n=14; STNx 1.2 ± 0.3 ng ml^{-1} h^{-1}, n=17). However, fetal plasma renin levels were lower in the STNx group (6.8 ± 3.0, n=17) than in the control group (15.1 ± 7.9 ng ml^{-1} h^{-1}, n=14, P=0.07).

Six ewes in each group received a high salt diet for 4 days i.e. they had access to 8 l day^{-1} of 0.17 mol l^{-1} NaCl instead of their normal drinking water. When both groups were combined, maternal plasma renin levels fell from 1.9 ± 0.4 to 0.5 ± 0.2 ng ml^{-1} h^{-1} (n=12, P<0.05). Interestingly, in the STNx ewes on the high salt diet, the increase in urinary sodium output was greater than the increase in sodium intake, so their sodium balance became negative. Fetal plasma renin levels rose from 10 ± 7.7 (n=6) before salt, to 19.3 ± 7.4 ng ml^{-1} h^{-1} (n=6) after salt (P=0.05 after log transformation of the data). By contrast, in the control ewes on the high salt diet, maternal sodium balance remained positive, and there was no change in fetal plasma renin levels (before salt 11.0 ± 5.2, n=5; after salt 12.8 ± 8.8 ng ml^{-1} h^{-1}, n=5).

It is concluded that the fetal renin angiotensin system was suppressed in this model of maternal renal dysfunction. The renin angiotensin system is essential for normal renal development (Guron & Friberg, 2000). Therefore, by suppressing this system, maternal renal dysfunction may impair fetal renal development and predispose the offspring to hypertension. Furthermore, fetuses whose mothers have renal impairment may be exposed to greater fluctuations in salt and water balance than those whose mothers have normal renal function.

Gibson, K.J., Karime, B.M., Zhou, Y.P., Boyce, A.C. & Lumbers, E.R. (2000). *Proceedings of the Australian Health and Medical Research Congress*, 1210.

Guron, G. & Friberg, P. (2000). *Journal of Hypertension,* 18:123-127.