Specific effects of cortisol on components of circulating and tissue renin angiotensin systems of fetal sheep

E.R. Lumbers[1], D.H. Hershco[1], A.C. Boyce[1], K.J. Gibson[1], J.H. Burrell[1], J. Wu[1], K.M. Moritz[2], [1]School of Medical Sciences, UNSW, Kensington, NSW, Australia, [2]Department of Anatomy and Cell Biology, Monash University, Clayton, VIC, Australia

The renin angiotensin system (RAS) is involved not only in blood pressure control and fluid and electrolyte balance but also in the development of organs like the kidney and heart. To compare the RAS between different tissues during development, components of the RAS were measured in blood, kidneys, hearts and placentae of 14 fetal sheep (aged 110-114 days). Because cortisol is a key hormone affecting maturation, the effects of 48h infusions of hydrocortisone succinate (8.4 mg/day) were studied in 7 of these fetuses. Five control fetuses received 0.15M saline; 2 received no infusion. Fetuses were chronically catheterized under general anaesthesia (1g thiopentone i.v; 1-3% halothane in oxygen) at least 5 days previously. At completion of the infusions, animals were killed with pentobarbitone sodium (3.5g).

Heart and placenta did not have renin mRNA. Low levels of renin-like activity were found in the heart but not in the placenta.

Aogen mRNA was highest in kidney and heart and lowest in the placenta ($P<0.005$). ACE activity was high in the placenta and kidney and less in the heart ($P<0.05$).

Cortisol (149 ± 45 nM) had no effect on plasma renin or Aogen but caused a rise in serum ACE ($P<0.01$). Cortisol had different effects on components of tissue RASs. Renal renin levels ($P<0.05$) were increased with cortisol treatment, but not renin mRNA. Renal ACE activity, Aogen, AT_1 and AT_2 mRNA were unchanged. Lung ACE activity was increased ($P<0.02$) and placental ACE was directly related to plasma cortisol ($P<0.03$). Placental AT_2 mRNA was less after cortisol ($P<0.03$); AT_1 and Aogen mRNAs were unchanged.

Cardiac Aogen mRNA was directly related to cortisol ($P<0.02$); cardiac ACE, AT_1 and AT_2 mRNAs and receptor densities were not affected.

Therefore cortisol selectively affects different components of tissue RASs. Some effects, eg stimulation of ACE, may contribute to its hypertensinogenic action. Other effects on tissue RASs may influence tissue growth and development.