Exposure to alcohol during fetal life causes persistent changes in vascular function and passive mechanical arterial wall properties in the offspring

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Prenatal alcohol exposure in late pregnancy in sheep causes stiffening of artery walls and changes in endothelial vasodilator function in the fetus. Our present aim was to investigate if these changes in vascular stiffness and function persist into postnatal life.

From d95-d135 of gestation (term ~145d), ethanol (0.75g/kg) was infused *i.v.* daily into ewes (n=7) over 1h, and control ewes (n=7) received saline. The lambs were born naturally and at 8 weeks after birth, pulse wave velocity (PWV) and baroreceptor sensitivity were measured *in vivo*. At 9 weeks after birth lambs were euthanized and small mesenteric, coronary, renal, femoral and cerebral arteries were isolated for testing of reactivity and wall stiffness using wire and pressure myographs.

Maternal and fetal plasma ethanol concentrations peaked at ~0.11g/dL 1h after infusion onset and declined to zero by 8h. Endothelium-dependent relaxation was impaired in femoral and renal arteries of ethanol-exposed lambs (P<0.001). This was attributed to a reduced contribution of nitric oxide in femoral arteries and to reduced contributions of vasodilator prostanoids and endothelium-derived hyperpolarizing factor in renal arteries. Smooth muscle relaxation evoked by the nitric oxide donor sodium nitroprusside was impaired in renal and femoral arteries, while smooth muscle contraction was unaltered in any of the arteries. Arterial wall stiffness was altered in most vascular beds of ethanol-exposed lambs. Some arterial beds exhibited increased stiffness while others were more compliant and these changes were sex-dependent. PWV and baroreceptor sensitivity were reduced in ethanol-exposed lambs (P=0.006 and 0.003, respectively).

Endothelial vasodilator dysfunction in ethanol-treated fetuses persists after birth in arteries from some vascular beds. The widespread arterial stiffening observed in ethanol-treated fetuses is altered postnatally, with some vascular beds having increased compliance, and these changes are associated with lower PWV. The persistent changes in postnatal vascular function and baroreceptor sensitivity induced by prenatal ethanol may increase the risk of cardiovascular disease in adulthood.