Early life environments and programming of the vascular phenotype

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Disturbances in the early life environment can have life long repercussions on cardiovascular health. Perturbations during critical times in development including fetal and early postnatal life can influence arterial structure and function, predisposing to cardiovascular disease. We have studied the effects of a variety of early life challenges on vascular function. Challenges investigated include vitamin D deficiency, several different models of intrauterine growth restriction, prenatal glucocorticoid or alcohol exposure, and the lactational environment. The striking finding to emerge from this work is that the nature of vascular dysfunction exhibits regional heterogeneity. Vascular mechanisms that are targeted include endothelial function, neuromuscular transmission, smooth muscle reactivity and wall stiffness. Of these mechanisms, we have found that a change in wall stiffness is generally the most consistent indicator that there has been an exposure to an early life insult. Intrauterine growth restriction causes stiffening of the coronary arteries of the fetal sheep. Alcohol exposure in the fetal sheep causes stiffening of arteries across the body. Some insults can also give rise to functionally opposing responses in different vascular beds. For instance, maternal alcohol intake results in endothelial vasodilator dysfunction in coronary arteries and hyperfunction in the mesenteric arteries of fetal sheep. Changes in vascular function that persist into adulthood increase the risk of cardiovascular disease. Seven year old sheep exposed to two days of prenatal glucocorticoids early in pregnancy had significantly increased coronary artery stiffness. Aged rats exposed to vitamin D deficiency during early life had persistent alterations in renal artery function including altered wall stiffness and augmented neurovascular constriction. The early postnatal environment can also influence vascular function. Changes in the lactational environment can either rescue or aggravate disturbances in vascular function caused by prenatal insults. Although not tested in all models, there appears to be sexual dimorphism in the nature and extent of vascular dysfunction, with males tending to have worse outcomes than females. In conclusion, a variety of early life insults can induce adaptations in the developing vasculature that may cause lasting alterations in function. Persistence of vascular dysfunction into adulthood will increase the risk of cardiovascular disease.