

## **Intrauterine growth restricted fetuses have increased blood flow to the adrenals and decreased blood flow to the heart but no difference in brain blood flow**

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Intrauterine growth restriction (IUGR) refers to the inability of a fetus to grow to its genetically determined potential size. IUGR fetuses are known to have an increased risk of cardiovascular disease in later life. The most common cause of IUGR is placental insufficiency, which is associated with a reduction in delivery of oxygen and/or nutrients to the fetus. It is well established that in response to acute hypoxemia, fetuses redistribute their cardiac output to maintain adequate perfusion of key organs including the brain, heart and adrenal glands at the expense of peripheral tissues. It is not known, however, whether the redistribution of cardiac output persists in chronically hypoxemic IUGR fetuses. The surgical removal of uterine caruncles (placental attachment sites) in the non-pregnant ewe results in the restriction of placental growth (PR) and chronic fetal hypoxemia. We hypothesize that exposure of the fetus to PR and chronic hypoxemia results in increased blood flow to the brain, heart and adrenals in late gestation. At  $123 \pm 1$  d gestation, vascular catheters were implanted in the fetuses to measure fetal blood gases, blood pressure (BP) and heart rate (HR). Blood flow studies were conducted at  $130 \pm 1$  d of gestation, using fluorescent labelled microspheres. At  $133 \pm 1$  d gestation (term  $150 \pm 3$  d), ewes and fetuses were humanely killed and fetal weights recorded. The fetal tissues including brain, heart and adrenals were dissected and weighed. Microspheres were harvested by tissue digestion and the amount of fluorescence in each organ was then quantified to measure blood flow. Fetuses were allocated into two groups: control (C) (n=6) and IUGR (n=5) according to their mean gestational PaO<sub>2</sub> and fetal weight. Fetal weight (C,  $3.7 \pm 0.1$  kg; IUGR,  $2.7 \pm 0.1$  kg) and mean gestational PaO<sub>2</sub> (C,  $21.8 \pm 1.4$  mmHg; IUGR,  $15.4 \pm 0.2$ ) were significantly reduced in the IUGR group. There was no difference in baseline MAP and HR between the control and IUGR fetuses. There was no difference in blood flow to brain between the two groups, however IUGR fetuses had a significantly higher blood flow to the adrenals and significantly lower blood flow to the heart compared to control fetuses. Reduction in heart blood flow in IUGR fetuses may be responsible for changes in cardiomyocyte and blood vessel development and increase the risk of cardiovascular disease in their adult life. Whereas the increase in blood flow to the adrenal may be necessary to support the increase in plasma cortisol concentrations in IUGR fetuses. The lack of change in brain blood flow in the IUGR fetus, who exhibits brainsparing is an unexpected finding but may reflect differences in substrate delivery, extraction or consumption in the brain of the IUGR fetus.