Why are endocrine disruptors important?

- Both animal livestock & humans are routinely exposed to a cocktail of environmental chemical pollutants. These include endocrine disrupting chemicals (EDCs) which can disrupt hormone synthesis or signaling.
- EDCs can enter the fetal compartment, potentially affecting development of fetal endocrine organs & programming of adult disease.
- Steroid hormones made in the fetal adrenal gland regulate the oestrogenic milieu of pregnancy, maturation of other fetal organs & onset of parturition, so that altered steroid hormone levels could disrupt these processes.
- EDCs are present in dried sewage sludge pellets, a biosolids product of soil water purification, commonly used as a fertilizer on livestock pasture.
- Texel sheep were chosen as a large animal model of EDC exposure due to their similar fetal development & gestation period to humans.
- The study aimed to compare steroidogenic gene expression in e110 ovine fetal adrenals from mothers exposed before or during pregnancy to pasture treated with sewage sludge or an organic fertilizer control.

Candidate genes & PTCHD-1, SHH, STAR, HSD3β2, HSD11β1, HSD11β2, CYP11A1, CYP17A1 & MR expression in e110 ovine fetal adrenals was determined by QRT-PCR, based on a literature search for key regulatory steps. Normally-distributed data was analysed by one-way ANOVA & Tukey’s post-hoc tests to assess significance.

CYP11A1 & HSD3β2 are significantly increased in CT vs other groups while CYP11A1 is also elevated, consistent with SSC-positive cell numbers.
- Both HSD11B1 & HSD11B2 are decreased in TT exposure versus CC control groups, while PTCHD1, SHH & MR are unchanged, suggesting they are unaffected by maternal or fetal EDC exposure.
- STAR, CYP11A1 & HSD3β2 catalysed key regulatory or rate-limiting steps in the steroidogenic pathway. EDC-mediated upregulation may lead to increased progesterone & elevated cortisol production in sheep and cortisol & adrenal androgens in humans. Decreased HSD11B1 may reduce oxidation of cortisol to cortisone, maintaining high cortisol.
- Samples were collected at e110 (ovine term = e144-151) when the fetal adrenal is regulated by pituitary ACTH, but before the normal prepartum surge in fetal steroid concentrations.

Discussion & conclusions

- Fetal adrenal steroids (cortisol in sheep, DHEAS in higher primates) play key roles in parturition, driving increases in maternal plasma oestrogen & other factors accompanying the onset of normal spontaneous term labour. Potentially, precocious EDC-mediated elevation of steroids could perturb fetal organ maturation & predispose to preterm birth.

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References:

QRT-PCR analysis of the effect of in utero exposure to sewage sludge on steroidogenic gene expression in the ovine fetal adrenal gland

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