IS THE BLUNTED INSULIN RESPONSE OF PREGNANT SHEEP DUE TO INCREASED NEFA CONCENTRATION?

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Mobilisation of maternal fat reserves, which results in increased non-esterified fatty acid (NEFA) plasma concentrations, is one of the homeorhetically regulated adaptions of pregnancy. Fat mobilisation, together with the development of insulin resistance in maternal liver and peripheral tissues (Petterson et al. 1993) as well as a reduction in pancreatic sensitivity to glucose (Regnault et al. 1993), may spare glucose for non-insulin dependent tissues in the sheep. Furthermore, in the rat, increased concentrations of NEFA have been shown to suppress *in vitro* glucose-stimulated insulin release (Elks 1993). We examined the effect of a glucose-induced reduction in plasma NEFA concentration and insulin release in fasted pregnant ewes to determine if the reduction in pancreatic sensitivity was related to NEFA concentration.

Three pregnant and five dry merino ewes at 135 days post-coitus were fitted with two indwelling jugular vein catheters and fasted for 20 hours. Blood samples were taken 30 and 15 min before beginning a primed (0.4g/kg) continuous infusion of glucose sufficient to maintain blood glucose at six-times basal concentration. Throughout the two hour infusion, samples were withdrawn at five minute intervals. Blood glucose concentration was monitored with Accutrend (Boehringer Mannheim) and the glucose infusion rate adjusted accordingly. Plasma samples were stored at 20°C for insulin and NEFA analysis.

Fig. 1

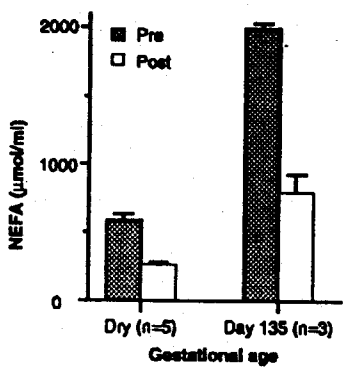
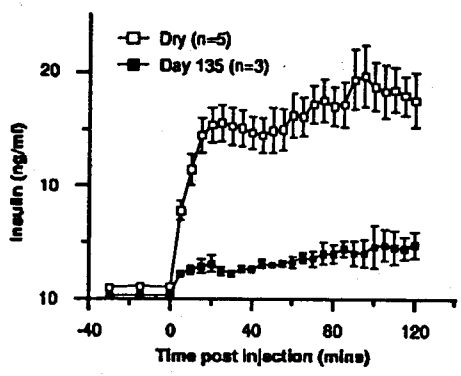


Fig. 2



The glucose infusion significantly ($P<0.001$) reduced plasma NEFA concentration in both dry and pregnant ewes (Fig. 1). However, plasma insulin concentration was significantly ($P<0.05$) reduced in pregnant ewes (Fig. 2). This data suggests that either NEFA concentration was not reduced sufficiently in pregnant ewes to overcome pancreatic insensitivity to glucose, or other factors of pregnancy, in addition to NEFA, are responsible for this blunted insulin response to glucose challenge.

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