

METABOLIC CONSEQUENCES OF IMMUNO-MODULATION OF HORMONES OF THE HYPOTHALAMO-PITUITARY-ADRENAL AXIS.

A.Z. SHAHNEH*, R.D.G. RIGBY**, R.M. HOSKINSON** AND P.C. WYNN*

Chronic elevation of circulating cortisol levels in response to stress is associated with depressed muscle protein accretion and increased fatness. This study describes various metabolic responses to chronic active immunization against the adrenal stimulatory hormone, ACTH. Groups of Border Leicester–Merino x Dorset Horn ewe lambs (n=8) were immunized with an ACTH–ovalbumin(OA; 1:2) conjugate emulsified in Freund's complete (primary) or incomplete (booster) adjuvant or adjuvant alone at 12, 18, 22 and 26 weeks of age. After weaning at 25 kg LW animals were maintained at pasture until 28 kg LW and thereafter offered a pelleted lucerne:oats ration (60:40) **ad libitum**. At 36 kg LW N balance was conducted for 7d and subsequently animals were fitted with indwelling jugular catheters. Blood samples were collected at intervals of 5–15 min for up to 6h to **assess** the metabolic and endocrine responsiveness of animals to either no stimulus (day 1), infusion with GH releasing factor (GHRF, 2 and 4 $\mu\text{g kg}^{-1}$: day 2) and glucose (200 and 400mg kg^{-1} :day 3) or exposure to the psychosocial stress of a barking dog (5 min: day 4). Plasma levels of hormones, antibodies and metabolites were measured by conventional radioimmunoassay, ELISA and autoanalytical techniques respectively. Animals were subsequently slaughtered and back fat and eye muscle area (EMA) assessed.

Anti-ACTH antibody titre reached $1/24500 \pm 7000$ 7 days after the second boost which resulted in a marked suppression in plasma cortisol levels compared with controls for the duration of the study. The growth rates were 190 ± 10 and $180 \pm 10 \text{ g d}^{-1}$ (mean \pm sem) and feed conversion efficiencies 8.29 ± 0.35 and $8.51 \pm 0.35 \text{ kg feed kg}^{-1}$ LW for control and immune groups respectively while N retention did not vary between groups. Plasma GH levels were stimulated 12 fold by the low GHRF dose in both groups and showed the same degree of somatotroph desensitization to the higher dose. Plasma insulin levels were depressed by 25% in the immune group, but not in the controls while urea levels were increased by 13% by GHRF in the control group only. Glucose infusion resulted in a similar dose dependent increase and subsequent decay in plasma glucose and insulin levels in both groups while circulating GH levels remained unaltered. ACTH immunization ablated the marked cortisol response to a barking dog observed in control animals. This **stressor** stimulated plasma GH levels by 32% in immune animals, but had the opposite response in the control group (45% decrease). Similarly the acute response in circulating insulin was more marked in the immune group, although the increase in glucose levels did not vary between groups. In terms of metabolic efficiency perhaps the most significant result was the 10 fold increase in plasma B endorphin levels observed in immune animals. The level of back fat was reduced also in this group (3.00 ± 0.42 v 4.33 ± 0.40 mm for controls), although EMA did not vary.

ACTH immunization alters the metabolic responsiveness of animals to psychological stress, although this appears not to be related directly to pancreatic or somatotroph sensitivity. This procedure decreases fat deposition, although the mechanism of action is not apparent.

This project was supported by the Meat Research Corporation

*Department of Animal Science, University of Sydney, Camden, NSW, 2570.

**CSIRO, Division of Animal Production, PO Box 239, Blacktown, NSW, 2148.