

estrogen-induced hernia formation. **Conclusion:** Taken together, our findings from the mild *Arom^{hum}* mouse model suggest that lower levels of estrogen excess in LAM are the primary driver of muscle atrophy and hernia formation because this mouse model do not exhibit circulating T deficiency. Our findings will constitute a starting point for dissecting the relative roles of estrogen and androgen action in inguinal hernia development. This has the potential to facilitate drug development to prevent and treat hernias, especially recurrent hernias after primary hernia repairs in vulnerable populations such as elderly men.

Neuroendocrinology and Pituitary HYPOTHALAMIC-PITUITARY DEVELOPMENT AND FUNCTION

Food Restriction Effects on the Hypothalamus-Pituitary-Gonadal Axis

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It is well known that nutritional status affects the reproduction, since an adequate amount of energy is necessary for puberty onset and fertility. However, the neural mechanisms by which energy homeostasis affects reproduction is not completely elucidated. To determine if acute or chronic food restriction (FR) are able to modulate the estrous cycle, adult female mice were used in the experiments. The estrous cycle was evaluated by daily observation of vaginal smear. To determine the effects of an acute FR protocol on estrous cycle, females were individualized and kept on *ad libitum* diet (control, n=17) or fasted for 24 hours (n=21). A subgroup of animals was euthanized shortly after the 24-hours test to collect hypothalamus and determine *Kiss1* mRNA levels, while another group of mice were regrouped and fed *ad libitum*. To determine the effects of a chronic FR protocol on estrous cycle, control mice were individualized and maintained with 100% of daily food content (average of 5 g per day, n = 6), or submitted to 60% of FR (n= 12). Animals were fed *ad libitum* after test. As expected, mice fasted for 24-hours exhibited a significant weight loss (control: 21.7 g \pm 0.5 vs 21.6 \pm 0.5 g; fasted: 22.7g \pm 0.5 vs 18.7g \pm 0.4, $P=0.0001$). This effect was followed by a significant reduction of hypothalamic *Kiss1* mRNA expression (control: 1.0 \pm 0.2; fasted: 0.3 \pm 0.05, $P=0.04$, n=4/4 per group). Surprisingly, even under lower *Kiss1* mRNA levels, 24-hours fasting induced no changes on estrous cycle. On the other hand, chronic FR induced a gradual weight loss (body weight at the 5th day of FR, control: 21.5g \pm 0.2; FR: 17.3g \pm 0.7, $P=0.0002$). The chronic FR was follow by the disruption of estrous cyclicity. While control mice exhibited a regular pattern of cyclicity during the period of evaluation, only leukocytes were identified in the vaginal smear of mice submitted to 60% of FR, even though they had a normal cycling pattern before the test. Therefore, by comparing 30 days of estrous cycle evaluation, including the period before chronic FR, while control mice exhibited cornified cells in the vaginal smear 58.5 \pm 4.9% of days, female mice submitted to FR exhibited cornified cells in 38.3 \pm 3.8% of days ($P= 0.0068$). Approximately 3-4 days

after the end of the chronic FR females returned to exhibit estrous cyclicity, however the length of the estrous cycle was prolonged compared to control group. Our data suggest that chronic nutritional status variations are required to disrupt the hypothalamus-pituitary-gonadal axis and therefore the estrous cyclicity.

Neuroendocrinology and Pituitary NEUROENDOCRINE & PITUITARY PATHOLOGIES

The Interaction Between Thiazide-Associated Hyponatremia and Acute Illness in Hospitalised Patients

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Thiazide diuretics, widely used in the management of hypertension, are associated with a five times greater risk of hyponatremia (serum Na <135mmol/L) than in the general population. Hyponatremia in hospitalised patients warrants special consideration since it is associated with increased morbidity and mortality.

The aim of this study was to describe the clinical characteristics and outcomes in acutely ill medical patients with thiazide-associated hyponatremia (TAH).

We performed a retrospective, case control study examining all acute, unselected medical admissions, over a six week period, to The Royal London Hospital. Cases were defined as adults admitted to hospital with TAH (hyponatremia and a history of being prescribed thiazide diuretic pre-admission). Each case was matched by age, gender and degree of hyponatremia to a similar control - admitted with hyponatremia and no pre-admission exposure to thiazide (non-TAH). Clinical characteristics and treatment outcomes were compared between TAH and non-TAH cohorts.

A total of 1,341 consecutive acute medical admissions (49.7% men) were evaluated. Hyponatremia was detected in 240 (17.9%) admissions. Median (\pm SD) length of stay was longer among patients with hyponatremia compared to normonatremic patients (5.0 \pm 12.4 versus 3.0 \pm 9.2 days; $p<0.0001$). In-hospital mortality was higher in the hyponatremic group (8.8% versus 4.4% $p=0.005$). Twenty-two cases (11 men) of TAH accounted for 9.2% of patients with hyponatremia. Median age 64 \pm 14 years was similar to other patients with hyponatremia 68 \pm 20 years. The median admission serum sodium for TAH cases was 131.5 mmol/L (IQR 126.8 - 134) with a discharge serum sodium of 136.5 mmol/L (IQR 133.8 - 139.3). When compared to matched controls, patients with TAH had similar presenting symptoms - most commonly confusion, headache and dizziness. Length of stay among TAH cases was similar to controls; 5.5 \pm 5.1 versus 4.0 \pm 3.7 days; $p=0.24$. Mortality (10%) was the same in both groups. Thiazide was withdrawn during admission in 14 (64%) cases.

In conclusion, acute, clinical outcomes for hospitalised patients with TAH are similar to those with comparable degrees of hyponatremia due to other causes.