Abstract

Individual feed consumption was determined in a group of ovariectomized rats. They were then divided into two groups, one restricted to 75% of their individual normal consumption and the other to 50% of normal. During a period of 19 days, the rats were injected with 2 μg EB plus 6 mg P to stimulate mammary gland growth, then sacrificed and DNA/100 g bw determined. In comparison with a group of 78 full-fed control rats, gland growth was depressed only 3.89%, a nonsignificant amount by 75% of their normal feed intake, and 17.84%, a reduction significant at the 1% level when restricted to 50% of their feed intake.

Variation in the normal feed consumption of female rats of the Sprague-Dawley-Rolfsmeyer strain has been studied in this laboratory. In the initial study, the mean feed consumption of 24 rats weighing an average of 265 g was 5.26 g/100 g body weight (bw), with a range from 4.2 to 5.7 g/100 g bw (3). Since the initial study, a total of 132 rats, with a mean weight of 235 g, have shown a normal frequency distribution around a mean of 5.7 g/100 g bw (6). In a study of the effect of feed restriction upon mammary gland growth, use of the mean feed intake as a base is subject to considerable error, because those animals normally consuming less than the mean would be restricted less and those eating more than the mean would be restricted more than indicated. In this study, the normal feed consumption of each animal was determined before the experiment was initiated. Then the feed of each animal was restricted to 75 or 50% of its normal intake.

The object of the present study was to determine the effect of feed restriction on the growth of the mammary glands of ovariectomized rats stimulated with estrogen and progesterone for 19 days.

Materials and methods

Adult rats of the Sprague-Dawley-Rolfsmeyer strain were ovariectomized 2 wk before being placed in individual metabolism cages so constructed as to prevent coprophagy and feed wastage. They were fed Purina Lab Chow with an energy value of 4.41 calories/gram and 23.4% total protein. After a three-day adjustment period, daily feed consumption was determined for seven days. Temperature was maintained at 25.5 ± 0.5 °C and the rats were artificially illuminated during daylight hours.

The rats were then divided into two groups of approximately equal body weight and feed consumption/day. To one group feed was restricted to one-half of their individual normal daily feed intake, whereas the second group received three-fourths of their previous normal intake.

Mammary gland growth was then stimulated by the daily injection of 2 μg of estradiol benzoate (EB) and 6 mg progesterone (P)/day for 19 days. On Day 20, the rats were sacrificed and their six posterior mammary glands removed and DNA determined by the method described (1).

For normal control data, a total of 78 ovariectomized rats have been administered 2 μg EB + 6 mg P for 19 days. The mean DNA/100 g bw of this group was 6.95 ± 0.32 (Table 1).

Results

The 21 rats fed three-fourths of their normal feed consumption of 5.74 g/100 g bw/day weighed 303.3 g at the beginning of the experiment. During the 20-day period their body weight was reduced to a mean of 277.7 g, a reduction of 8.4%. The mean DNA of the mammary glands was 6.68 mg/100 g bw, based on the initial body weight, or 7.30 mg based on the final body weight (Table 1). In comparison with the control group on full feed, this is a decrease of 3.89%. Compared to the control group, this difference is not significant at 1 or 5%.

The 23 rats fed one-half of their normal feed intake of 5.96 g/100 g bw/day weighed 295.4 g at the beginning of the experiment and 232.1 g at the end of 20 days. This is a loss of 63.3 g;
The mean DNA of the mammary glands was 5.71 mg/100 g bw, based on the initial body weight, or 7.27 mg based on the final body weight. In comparison with the control group on full feed, this is a decrease of 17.84%. This is significant at 1% level. Comparison of DNA of three-fourths- and one-half-fed rats is significant at the 5% level, but not at the 1% level.

It will be noted that the group of control rats weighed a mean of 264 g, compared to 303 and 295 g for the experimental groups. This was done to ensure that the restricted feeding program would not reduce their body weight greatly below that of the control group. It should be pointed out that variation in body weight of the rats is equalized by expressing the total DNA in terms of 100 g body weight.

**Discussion**

It has been recognized for many years that underfeeding tends to depress the secretions of the anterior pituitary and their target glands other than ACTH and the glucocorticoids. The problem of reduced feed intake upon mammary gland development was studied years ago by Sykes et al. (11). In their study feed was restricted 30% in comparison with pair-fed controls from weaning time until the end of pregnancy. They observed a reduction of 22.6% in body weight and an 80% reduction in gland weight. While part of the reduction in gland weight was probably due to a reduction in the fatty pad in which the gland develops, it was suggested that part of the reduction was due to reduced mammary gland development. In the present study, by the estimation of DB:A, it is possible to determine directly the effect of reduced feed consumption on mammary gland lobulealveolar growth.

It was shown recently that a 22% reduction in feed caused a 13% reduction in 14 days and 42% in 27 days of the thyroid hormone secretion rate (TSR). On a 48% reduction in feed, a reduction of 28 and 54%, respectively, was observed in TSR (2). Quantitative data on the effect of underfeeding in the rat on the hormone secretion rates of other hormones are unavailable.

While estrogen and progesterone are recognized as the primary stimulants of mammary gland growth during pregnancy, it has been shown that L-thyroxine (L-T4) synergizes with these hormones to stimulate increased mammary gland DNA (9). It has been shown, also, that bovine GH stimulated a slight but not significant increase in DNA (7). While insulin secretion...
is not under direct anterior pituitary control, it has been shown that alloxan diabetes depressed and insulin stimulated mammary gland growth in rats (8).

Ovariectomized rats stimulated with estrogen and progesterone have shown considerable variation in the DNA content of their mammary glands/100 g bw (9). It has been suggested that part of this variation may be due to variation in the normal hormone secretion rate.

If feed restriction does depress the secretions of the anterior pituitary and its target glands this would, in itself, depress feed consumption. During a period of 6 to 13 days after hypophysectomy, it was shown that feed intake was reduced 28.3% (5). After thyroparathyroidectomy of 10 to 16 days, feed reduction of 13% was observed, and after adrenalectomy a reduction of 27.12%. When both glands were removed, feed consumption was reduced 30.5% in 11 to 17 days (4).

It has been claimed that hypophysectomy totally depresses lobule-alveolar growth (10), but data on growth as measured by DNA are not available. However, after adrenalectomy, the mean DNA/100 g bw was reduced to 4.64 mg, over 1 mg lower than the group on one-half feed (1). Alloxan diabetes in rats has been shown also to depress mean total DNA to 4.5 mg/100 g bw (8), even though feed consumption was increased.

It would appear that feed restriction up to 50% during a period of 19 days and under the stimulus of estrogen and progesterone has a less depressing effect on mammary gland growth, as measured by DNA, than removal of some endocrine glands or the absence of their hormones.

References