

## Production of Nitrogen Retention in Hypophysectomized Rats by Small Doses of Hypophyseal Growth Hormone.\*

LESLIE L. BENNETT, CHOH HAO LI, AND BARBARA LAUNDRIE.

*From the Institute of Experimental Biology and the Division of Physiology, University of California, Berkeley, Calif.*

Previous work from this laboratory has demonstrated that the administration of 1 mg per day of pure hypophyseal growth hormone will produce nitrogen retention and weight gain in normal adult female rats<sup>1</sup> and that .01 mg per day will produce weight gain in *ad libitum* fed hypophysectomized rats.<sup>2</sup> This present study was undertaken to determine whether the administration of such small amounts of growth hormone would produce a demonstrable nitrogen retention in hypophysectomized rats.

**Methods.** Ten male rats of the Long-Evans strain were used as the experimental animals. They were hypophysectomized through the parapharyngeal approach when they were between 58 and 65 days of age. Following hypophysectomy they were maintained in individual metabolism cages and their average *ad libitum* food intake<sup>†</sup> was determined for 11-13 days. Daily urine collections were started 11-13 days after hypophysectomy and the urine was analyzed for total nitrogen by the Kjeldahl procedure.

During the entire urine collection period each rat was fed daily a weighed amount of diet which was the same or slightly less than

the rat's average daily consumption during the previous post-hypophysectomy period. Thus the food consumption of each rat was nearly constant throughout the entire experimental period and was restricted in amount.

Urine was collected for a 10-day control period prior to growth hormone injection and for a 4-day control period after cessation of injection. The growth hormone used was prepared according to the previously published method<sup>3</sup> and was administered twice daily intraperitoneally. It was given at dose levels of .05 mg, .03 mg and .015 mg daily.

**Results.** The data from the experiment are presented graphically in Fig. 1 and analyzed statistically in Table I. It will be seen that during the growth hormone injection period there was a slight increase in average food intake. This was due to the fact that only occasionally did a rat fail to consume completely the food that was offered. In spite of the slight increase in food consumption, and hence nitrogen intake, there was a decrease in the average urinary output of nitrogen during the administration of growth hormone at all dose levels. The largest dose of growth hormone, 50  $\gamma$  per day, produced the greatest nitrogen retention, 53 mg per day. The smallest dose of growth hormone, 15  $\gamma$  per day, produced the least nitrogen retention, 17 mg per day. As demonstrated by Fig. 1, during the injection period of 15  $\gamma$  of hormone per day the amount of urinary nitrogen excreted the first day was less than the amount excreted the following days. This undoubtedly reflects a continuing effect of the

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<sup>1</sup> Gordan, G. S., Bennett, L. L., Li, C. H., and Evans, H. M., *Endocrinology*, 1948, **42**, 153.

<sup>†</sup> The diet fed consisted of ground whole wheat 67.5%, casein 15.0%, whole milk powder 10.0%, NaCl 0.75%, CaCO<sub>3</sub> 1.5%, hydrogenated vegetable oil (Crisco or Primex) 5.25%. To each kg of diet were added 3.5 g of Sardilene (fish oil concentrate containing 3000 USP units vitamin A and 400 Chick Units vitamin D per g).

<sup>2</sup> Li, C. H., Evans, H. M., and Simpson, M. E., *J. B. C.*, 1945, **159**, 353.

<sup>3</sup> Fisher, R. A., *Statistical Methods for Research Workers*, 10th Ed., Edinburgh, London, Oliver and Boyd, 1946.

Daily Food Consumption and Urinary Nitrogen Excretion of  
Hypophysectomized Rats Treated With Growth Hormone

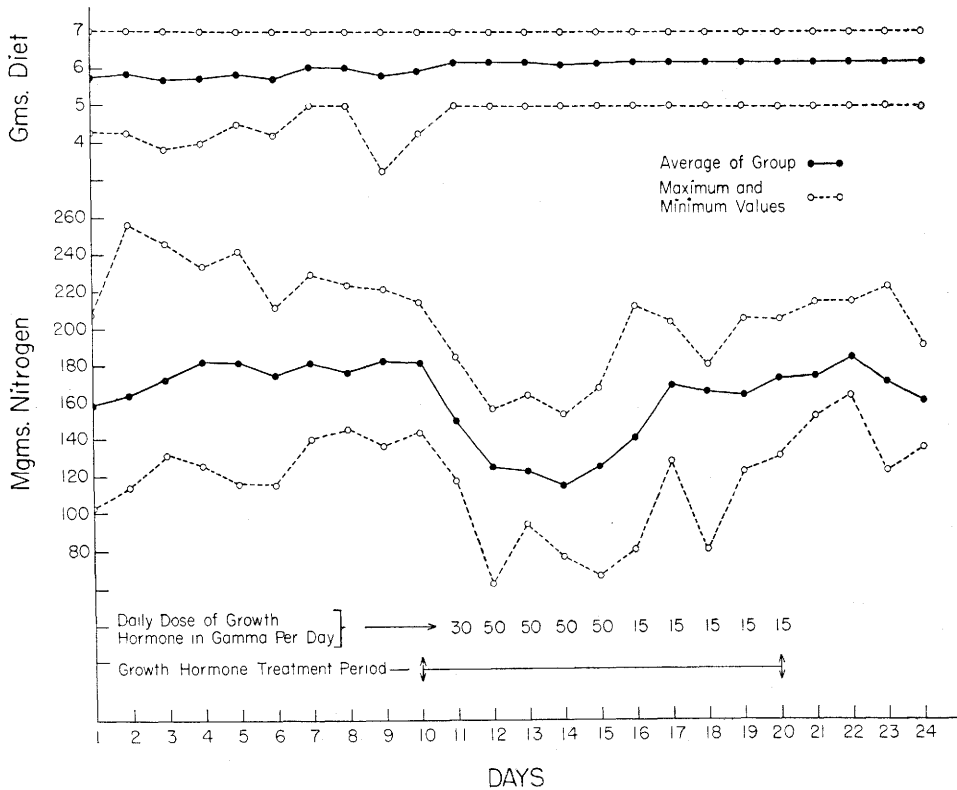


FIG. 1.

previous larger dose. If this day is omitted in calculating the averages the effect of the 15  $\gamma$  dose is not significant. The intermediate dose, 30  $\gamma$  per day, produced an intermediate effect. After the cessation of injection the urinary nitrogen excretion returned to its

original level.

*Conclusion.* Growth hormone administration in amounts as small as 30  $\gamma$  per day produces nitrogen retention in hypophysectomized rats maintained on a constant and restricted food intake.

TABLE I.  
Average Daily Food Intake and Urinary Nitrogen Excretion of Hypophysectomized Rats  
Treated with Growth Hormone.

| Daily dose<br>growth hormone  | Food intake,<br>g | Urinary nitrogen,<br>mg | p†  |
|-------------------------------|-------------------|-------------------------|-----|
| None (pre-injection control)  | 5.84              | 176 $\pm$ 3.1* (100)†   |     |
| .015 mg                       | 5.83              | 159 $\pm$ 4.2 (50)      | .01 |
| .030 mg                       | 6.12              | 151 $\pm$ 7.4 (10)      | .02 |
| .050 mg                       | 6.16              | 123 $\pm$ 4.3 (40)      | .01 |
| None (post-injection control) | 6.20              | 173 $\pm$ 3.4 (40)      | .70 |

\* Standard deviation of the mean.

† Number of observations in group.

‡ From Fisher's<sup>3</sup> table of t.