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THE EFFECT OF ANTERIOR PITUITARY GROWTH HORMONE UPON THE COMPOSITION OF GROWTH.[1]

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Certain extracts of the anterior pituitary body are now well known to produce unusual growth when administered to experimental animals and to human pituitary dwarfs. The physiologic or metabolic mechanisms through which these effects are produced are not yet known, however. In the experimental work described here the growth responses and the composition of the gains in weight were determined in rats treated with the hormone and maintained upon a limited food allowance.

Twelve groups of animals, each composed of litter-mates of the same sex, and initial body weight and length were used. One rat of each group became a control, a second received growth hormone and a third mate was killed and analyzed at the beginning of the experimental period. The control and its treated mate were fed daily the same amounts of food, according to the so-called "paired-feeding" technic developed by Mitchell.[2] The period of paired feeding and treatment ranged from eight to eleven weeks at the end of which the rats were killed by pairs and analyzed for water, fat, nitrogen and ash.

The anterior lobe extract used was prepared from fresh beef pituitary glands, purified and assayed. The amount injected daily was somewhat less than that necessary to cause a maximal growth response.

After treatment began the animals receiving the hormone immediately passed their control mates in weight and continued to show an excess gain each week until killed. The twelve

[1]Summary of paper presented before the Ohio Academy of Science, April 14, 1933, as part of a Symposium on Endocrinology.

[2]Mitchell, H. H. and J. R. Beadles. J. Nutrition, 2: 225. 1930.

controls weighed 2,382 grams initially and gained 764 grams; their twelve treated mates weighed 2,358 grams initially and gained 1,295 grams. The treated animals, on the same food consumption as their controls thus showed an excess gain of 531 grams, equivalent to the weight of two extra adult animals. Individually, eleven of the twelve treated rats showed an excess gain, a result which would be expected to occur by chance, only once in 340 times. The treated animals also showed significant excess gains in body length. By the technic of paired-feeding the amount of food given daily to the two members of any pair was determined by the appetite of the less hurgry member. In only 91 of 763 daily instances was a control rat more hungry than its treated mate.

The initial composition of both groups of animals estimated from the analyses of their litter mates, was: water, 62.0 per cent; fat, 12.7 per cent; nitrogen, 3.3 per cent; ash, 4.3 per cent; and energy, 2.33 calories per gram. The final composition of the controls was: water, 58.0 per cent; fat, 19.1 per cent; nitrogen, 3.0 per cent; ash, 4.0 per cent; energy, 2.83 calories per gram. The final composition of the treated animals was: water, 62.5 per cent; fat, 12.9 per cent; nitrogen, 3.2 per cent; ash, 4.1 per cent; energy, 2.32 calories per gram. The controls showed the characteristic changes in body composition with age that would be expected. These changes were statistically significant decreases in the proportions of water, nitrogen, ash and fat-ash-free dry tissue, and increases in the percentage of fat and in the heat value of the carcass. The treated animals, on the other hand, retained almost exactly their initial composition in all constituents and in the heat value of their tissues. Their gains in weight were consequently also closely similar to their carcass composition initially. The composition of the gains in weight, and of the excess gains by the treated rats is given in the accompanying table.

Statistical analysis of the data by Fisher's[3] measure of the significance of the difference in the means of small samples supports the inference that nitrogen and fat-ash-free dry tissue (protein) were the constituents most specifically affected by the hormone.

The nitrogen, ash and energy balances were determined in each group of animals, both directly from carcass analysis and

[3]Fisher, R. A. Statistical Methods for Research Workers. 3rd. Ed., London, 1930.

indirectly from the intake and excretion. The excess retention for the whole period by the treated rats over their controls was 22.5 grams of nitrogen and 22.4 grams of ash. The excess nitrogen retention by weeks closely paralleled the weekly excess gain in weight. The energy balance was slightly in favor of the controls, as they retained 341 calories (0.8 per cent of the total intake), more than their treated mates, despite the fact that their weight gain was some 500 grams less. The energy require-

TABLE I.

SUMMARY OF GAINS AND COMPOSITION OF GAINS IN CONTROL AND TREATED ANIMALS.

Group	Body Length Cm.	Live Body Weight Gm.	Empty Carcass Weight Gm.	Composition of Empty Carcass Gain Grams and Per Cent					Energy Calories
				Water	Ether Ext.	Fat-free Dry Tissue	Total N.	Ash	
CONTROLS—									
Total Gain	18.2	764	716	324	281	111	15.4	22.7	3161
Percent of Gain in Empty Carcass Weight				45.2	39.3	15.5	2.15	3.16	4.41*
Percent of Initial Datum	7.4	32.1	31.3	22.8	96.7	19.2	20.7	23.1	59.3
TREATED—									
Total Gain	33.1	1295	1217	771	162	284	37.9	45.1	2820
Percent of Gain in Empty Carcass Weight				63.3	13.3	23.4	3.12	3.71	2.32*
Percent of Initial Datum	13.5	54.9	53.7	54.9	56.3	49.6	51.5	46.4	53.5
EXCESS GAIN OF TREATED	14.9	531	501	447	—119	173	22.5	22.4	—341
Percent of Excess Empty Carcass Weight				89.2	—23.8	34.5	4.49	4.47	—0.68*

Empty carcass is the carcass minus the contents of the alimentary tract.
*Calories per gram of empty carcass weight.

ments for muscular activity were somewhat greater in the treated, but their energy expenditure per gram of weight gained was considerably less than that of the controls.

It is concluded that although the amount of the food consumption may be a limiting factor for growth under certain conditions, the growth hormone through its influence upon metabolic processes, is able to affect growth independently of the food intake. The growth produced has the same characteristics as the growth exhibited by young animals—a marked retention of nitrogen, synthesis and deposition of protein and a relatively high content of water and low content of fat.