GROWTH CHARACTERISTICS OF INTACT AND HYPOPHYSECTOMIZED FEMALE HAMSTERS. THE EFFECT OF BOVINE GROWTH HORMONE ON HYPOPHYSECTOMIZED HAMSTERS

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Post-weaning growth data, including body length, body weight, and several visceral organ weights, were collected for intact and hypophysectomized female hamsters aged 4 to 12 weeks. In addition, hypophysectomized hamsters were treated with bovine growth hormone for a period of six weeks and the effects examined.

INDEX WORDS: Hypophysectomized hamsters, bovine growth hormone, *Cricetus*

Weight measurements for the body and principal visceral organs have been recorded to study growth characteristics in several laboratory animals, including rats (Freudenberger, 1932, 1933; Zucker *et al.*, 1941; Zucker and Zucker, 1942; Webster *et al.*, 1947), guinea pigs (McPhee and Eaton, 1931; Webster and Liljegren, 1949), mice (Ogle, 1934), and chickens (Gilbreath and Upp, 1952; Breneman, 1941). In spite of the widespread use of the Syrian golden hamster for biological studies, the literature dealing with the fundamental measurements of this animal is scanty (Bond, 1945; Poiley, 1950), and the influence of pituitary growth hormone on the growth of hypophysectomized hamsters has never been examined. On the other hand, studies on the growth-promoting effect of BGH* in the hypophysectomized rat (Simpson *et al.*, 1949; Li *et al.*, 1949; Becks *et al.*, 1949) and mouse (Lostroh and Li, 1958) have previously been described.

This investigation was undertaken in order to secure information about the growth characteristics of both intact and hypophysectomized hamsters. The effect of BGH treatment was also conducted in the hypophysectomized hamster.

* Abbreviation: BGH, bovine pituitary growth hormone.

Materials and Methods

Immature female syrian golden hamsters (*Mesocricetus auratus*) were purchased from the local breeder at four weeks of age. The animals were randomly selected and divided into two groups: one to be hypophysectomized and the other for an intact control. Hypophysectomy was performed at 28 days of age by a parapharyngeal approach (Smith, 1930) after a tracheotomy under ether anesthesia. These animals were fed ad lib with a special white diet (Simonsen Lab., Gilroy, Calif.) and tap water, and autopsied at 4, 5, 6, 7, 8, and 12 weeks old in order to measure body length, body weight, and individual visceral organ weights for the heart, liver, kidneys, thymus, spleen, thyroid, pancreas, adrenals, ovaries, and uteri.

Growth hormone was isolated from bovine pituitaries by a procedure previously described (Li, 1954). The growth hormone (Fraction B) was dissolved in solutions of pH 9.0, and 0.2 ml of the hormone solution containing 25, 100 or 200 micrograms of BGH was injected intraperitoneally daily in the hypophysectomized hamsters, beginning on the 14th day after operation and continuing for 42 days. All experimental animals were weighed and had body length measurements taken weekly. At the end of the experiment, the animals were anesthetized with an intraperitoneal injection of 0.5 ml pentobarbital. The sella turcica was checked for the possible presence of pituitary fragments and the organs were carefully weighed. Statistical calculations were performed on an IBM 360 computer using a Fortran IV program to evaluate the significance of quadratic or linear regression between weights and ages, or weights and hormonal doses. For organ weights, the statistical data were obtained from values of absolute body weights.

Results

As shown in Table 1, the growth of body length and body weight in the intact female showed a positive linear regression to the logarithmic age and a positive quadratic regression to the absolute age. The growth of heart, liver, kidney, thyroid, and adrenals followed the same pattern, increasing their weights. The weights of the spleen, pancreas, thyroid, and ovaries also increased with the advance of age to show positive regression between the organ weight and the age. The thymus weight, however, reduced with the increase of age to show

TABLE 1

BODY LENGTH, BODY WEIGHT, AND ORGAN WEIGHTS[a] OF THE INTACT FEMALE HAMSTER

	Age (weeks)						Regression[b] Age		Regression[b] Log (age)	
	4	5	6	7	8	12	Quad.	Lin.	Quad.	Lin.
No. of animals	8	6	10	6	11	6				
Body length (cm)	13.6 ± 0.1	14.2 ± 0.1	14.8 ± 0.1	15.3 ± 0.1	16.0 ± 0.2	17.2 ± 0.1	S	(—)	N	S
Body weight (gm)	55.0 ± 2.4	63.0 ± 1.4	76.8 ± 2.5	91.3 ± 2.1	95.5 ± 2.1	119.2 ± 4.1	S	(—)	N	S
Organ weights (mg)										
Heart	183 ± 8 (0.33)	224 ± 3 (0.36)	255 ± 6 (0.33)	299 ± 7 (0.33)	316 ± 11 (0.33)	388 ± 14 (0.33)	S	(—)	N	S
Liver	3367 ± 95 (6.12)	4000 ± 139 (6.35)	4019 ± 181 (5.23)	4934 ± 327 (5.40)	4837 ± 385 (5.07)	4810 ± 197 (5.04)	S	(—)	N	S
Kidneys	613 ± 19 (1.12)	633 ± 6 (1.01)	700 ± 17 (0.91)	744 ± 26 (0.82)	772 ± 21 (0.81)	808 ± 18 (0.68)	S	(—)	N	S
Thymus	70.7 ± 2.4 (0.13)	70.4 ± 4.9 (0.11)	67.0 ± 3.0 (0.09)	68.4 ± 3.9 (0.08)	64.4 ± 2.6 (0.07)	63.8 ± 2.4 (0.05)	N	S	N	S
Spleen	90.0 ± 5.1 (0.16)	110.3 ± 7.9 (0.18)	109.9 ± 10.0 (0.14)	109.4 ± 12.0 (0.12)	118.9 ± 4.6 (0.13)	162.0 ± 12.0 (0.14)	N	S	N	S
Pancreas	228 ± 14 (0.52)	298 ± 15 (0.47)	312 ± 21 (0.41)	381 ± 16 (0.42)	376 ± 8 (0.39)	407 ± 16 (0.34)	N	S	N	S
Thyroid	1.6 ± 0.1 (0.0029)	2.6 ± 0.2 (0.0041)	2.9 ± 0.3 (0.0038)	3.9 ± 0.2 (0.0043)	3.9 ± 0.3 (0.0041)	4.1 ± 0.3 (0.0034)	S	(—)	S	(—)
Adrenals	6.5 ± 0.1 (0.012)	9.0 ± 0.3 (0.014)	10.2 ± 0.4 (0.013)	12.3 ± 0.7 (0.014)	14.5 ± 0.5 (0.015)	16.0 ± 0.7 (0.013)	S	(—)	N	S
Ovaries	19.6 ± 1.5 (0.036)	19.7 ± 1.1 (0.031)	26.3 ± 1.9 (0.034)	22.1 ± 3.5 (0.024)	25.6 ± 2.0 (0.027)	29.3 ± 2.2 (0.025)	N	S	N	S
Uteri	84 ± 7 (0.15)	164 ± 27 (0.26)	222 ± 23 (0.29)	165 ± 19 (0.18)	185 ± 29 (0.19)	242 ± 43 (0.25)	N	N	N	N

[a] Values in mean ± SEM; values in parentheses are percentage of body weight.
[b] Quad, quadratic; lin., linear; N, not significant; S, significant; (—), since quadratic regression is significant, the assumption of linearity is not accepted.

TABLE 2

BODY LENGTH, BODY WEIGHT, AND ORGAN WEIGHTS[a] OF THE HYPOPHYSECTOMIZED FEMALE HAMSTER

	Age (weeks)					Regression			
						Age		Log (age)	
	5	6	7	8	12	Quad.	Lin.	Quad.	Lin.
No. of animals	5	10	5	6	11				
Body length (cm)	13.5 ± 0.3	13.5 ± 0.1	13.8 ± 0.2	14.0 ± 0.1	14.4 ± 0.2	N	S	N	S
Body weight (gm)	55.8 ± 4.1	62.5 ± 1.4	62.8 ± 2.7	74.8 ± 2.8	80.0 ± 2.1	N	S	N	S
Organ weights (mg)									
Heart	181 ± 9 (0.32)	167 ± 6 (0.27)	161 ± 3 (0.26)	210 ± 5 (0.28)	196 ± 8 (0.24)	N	N	N	N
Liver	2879 ± 231 (5.16)	3333 ± 99 (5.33)	2563 ± 304 (4.08)	3328 ± 263 (4.45)	2768 ± 100 (3.43)	N	N	N	N
Kidneys	465 ± 23 (0.83)	458 ± 12 (0.73)	357 ± 7 (0.59)	490 ± 15 (0.66)	395 ± 18 (0.49)	N	N	N	N
Thymus	50.4 ± 6.0 (0.090)	44.5 ± 3.2 (0.071)	42.1 ± 2.6 (0.067)	43.0 ± 3.4 (0.057)	39.4 ± 4.1 (0.049)	N	N	S	(—)
Spleen	91.9 ± 12.4 (0.17)	68.3 ± 4.8 (0.11)	59.8 ± 8.4 (0.095)	66.1 ± 5.7 (0.088)	66.4 ± 3.2 (0.082)	S	(—)	N	N
Pancreas	205 ± 16 (0.37)	218 ± 13 (0.35)	184 ± 9 (0.29)	186 ± 17 (0.25)	183 ± 12 (0.23)	N	N	N	N
Thyroid	1.8 ± 0.2 (0.0032)	1.9 ± 0.2 (0.0030)	2.1 ± 0.2 (0.0033)	2.7 ± 0.2 (0.0036)	2.9 ± 0.3 (0.0036)	N	S	N	S
Adrenals	4.8 ± 0.2 (0.0086)	5.1 ± 0.2 (0.0082)	5.1 ± 0.1 (0.0081)	7.2 ± 0.4 (0.0096)	6.5 ± 0.1 (0.0080)	N	N	N	N
Ovaries	6.5 ± 0.6 (0.012)	5.5 ± 0.5 (0.0088)	5.3 ± 0.4 (0.0083)	5.7 ± 0.5 (0.0076)	5.7 ± 0.3 (0.027)	N	N	N	N
Uteri	17.9 ± 0.7 (0.032)	24.9 ± 1.3 (0.040)	18.1 ± 1.8 (0.029)	26.1 ± 1.3 (0.035)	21.4 ± 1.4 (0.027)	N	N	N	N

[a] Values in mean ± SEM; the values in parentheses are percentages of body weight.

[b] Quad, quadratic; lin., linear; N, not significant; S, significant; (—), since quadratic regression is significant, the assumption of linearity is not accepted.

a negative regression. Although the uterine weight appeared to have no regression to the age, the increase in weight from 4 to 5 weeks old was significant by t-test, but not so at a later stage of life.

When the absolute value of each organ weight had been calculated as relative percentage weights of body weight, the change in the relative organ weights of the heart, adrenals, and uteri did not appear to be significantly related with the advance of age. Nevertheless, the relative organ weights of most visceral organs such as the liver, kidney, thymus, pancreas, and ovaries decreased with aging to show negative regression between the weight and age.

Following hypophysectomy at four weeks of age in the female hamster, the growth of either body length or body weight was subse- and Figure 1). Similar to body length and weight, the thyroid weight quently reduced in rate but was not completely inhibited (Table 2

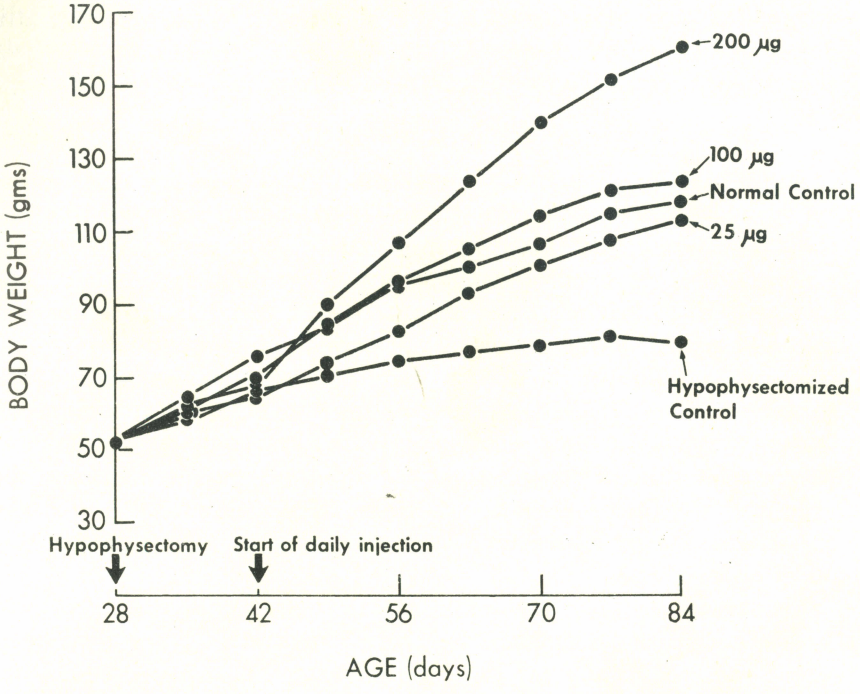

FIGURE 1

Average body weight curves of BGH injected (three daily doses of 25 µg, 100 µg, and 200 µg) hypophysectomized female hamsters compared with that of uninjected hypophysectomized controls and normal controls.

also increased with the advance of age to show a positive regression. On the contrary, the organ weights for the thymus and spleen decreased with age to demonstrate characteristic negative regressions. After sharp drops from 4 to 5 weeks after the hypophysectomy, most visceral organs, such as the heart, liver, kidneys, pancreas, adrenals, ovaries, and uteri, did not show further changes in weight. Regression analysis of the relative organ weights indicated that the percentage body weights of the heart, liver, thymus, spleen and pancreas reduced significantly with an increase in age. In contrast, the relative weight of the thyroid in the hypophysectomized animal increased significantly with age.

After treating the hypophysectomized animals with BGH for 42 days the body length, body weight, and organ weights of all visceral organs increased significantly to show positive regressions to the hormonal doses (Table 3 and Figure 1). The regression lines were linear to absolute doses or logarithmic doses in most cases. The relative organ weights of the heart, pancreas, spleen, and ovaries were also significantly regressive to the increase of doses.

Discussion

Brody and Ragsdaly (1922) have shown that there are three growth cycles in warm blooded animals: first a relatively rapid growth rate, then tapering off up to maturity, and finally either very slow increases or actual decreases during senility. A number of equations have been employed to fit these growth characteristics, however, most of these were not adaptable for the entire life period. The logarithmic equation was only suitable for the earlier phase of growth in the mouse (MacDowell *et al.*, 1927, 1930) and rat (Zucker and Zucker, 1942). In the present report, the post-weaning growth data on body length, body weight, and visceral organ weight for the intact female hamsters were examined for their quadratic or linear regression to the increase of either absolute or logarithmic ages according to a Fortran IV computer program.

Measurements from the intact female hamsters showed that body length, body weight, and the weights of visceral organs except heart, spleen, adrenals and uteri have a significant linear regression to the logarithmic age. Thus, the general growth figures for either body or visceral organs appeared to be exponentially proportional to the ad-

TABLE 3

GROWTH OF BODY AND VISCERAL ORGANS FOLLOWING DAILY INJECTIONS OF BGH FOR 42 DAYS IN HYPOPHYSECTOMIZED FEMALE HAMSTERS[a]

	Doses of BGH (μg)				Regression[b] Dose		Log (Dose +1)	
	0	25	100	200	Quad.	Lin.	Quad.	Lin.
No. of animals	6	5	5	5				
Body length (cm)	14.4 ± 0.1	16.8 ± 0.6	17.3 ± 0.1	18.2 ± 0.7	N	S	N	S
Body weight (gm)	83.4 ± 3.2	116.3 ± 2.4	129.8 ± 4.0	167.5 ± 2.8	N	S	N	N
Absolute organ weights, mg								
Heart	202 ± 15 (0.24)	351 ± 12 (0.30)	424 ± 21 (0.33)	506 ± 17 (0.30)	N	S	N	S
Liver	2904 ± 140 (3.48)	6565 ± 214 (5.65)	7454 ± 240 (5.74)	9299 ± 314 (5.55)	N	N	N	N
Kidneys	433 ± 20 (0.52)	718 ± 5 (0.62)	832 ± 54 (0.64)	997 ± 47 (0.60)	N	S	N	N
Thymus	38.0 ± 2.4 (0.046)	64.0 ± 3.4 (0.058)	67.1 ± 4.1 (0.049)	72.3 ± 4.5 (0.043)	N	S	N	N
Spleen	68.9 ± 3.3 (0.083)	202.0 ± 14.2 (0.17)	253.2 ± 29.1 (0.20)	272.4 ± 45.6 (0.16)	N	N	N	S
Pancreas	205 ± 8 (0.25)	422 ± 28 (0.36)	729 ± 66 (0.37)	603 ± 38 (0.36)	N	N	N	N
Thyroid	3.3 ± 0.2 (0.0042)	3.2 ± 0.3 (0.0028)	3.7 ± 0.5 (0.0029)	4.7 ± 0.5 (0.0028)	N	N	N	S
Adrenals	6.1 ± 0.5 (0.0073)	8.8 ± 0.4 (0.0076)	11.7 ± 0.7 (0.0090)	10.9 ± 0.7 (0.0065)	N	N	N	N
Ovaries	6.1 ± 0.5 (0.0073)	9.6 ± 0.5 (0.0083)	12.2 ± 1.2 (0.0093)	21.0 ± 2.0 (0.013)	N	S	N	N
Uteri	20.5 ± 1.7 (0.025)	48.0 ± 4.1 (0.041)	77.3 ± 6.0 (0.060)	66.6 ± 7.0 (0.040)	N	N	N	N

[a] Values in mean ± SEM; the values in parentheses are percentages of body weight.

[b] Quad, quadratic; lin., N, not significant; S, significant; (—), since quadratic regression is significant, the assumption of linearity is not accepted.

vance of the absolute age. The lack of significant regression between the uterine weight and age during the whole experimental period, and the existence of a significant increase in the organ weight from 4 to 5 weeks old at the earlier stage of the experiment suggests the extraordinary early arrival of the growth plateau in this particular sex organ. The striking difference between regular visceral organs and the thymus with regard to their growth characteristics is the increase of the organ weight in the former, and the decrease in that in the latter with the advance of age. Despite the increase of absolute weight in most visceral organs during development, the relative percentage of organ per body weight was decreasing in all cases with the advance of age. Apparently, the growth of most visceral organs was chiefly controlled by the pituitary hormones. Following hypophysectomy the characteristic exponential growth of organs such as the heart, liver, and kidney ceased or reversed (Table 2). However, hypophysectomy could not reduce the positive growth rate in body length and body weight (Figure 1 and Table 2).

Significant regression of body length and body weight to the hormonal doses were observed in the hypophysectomized animals following BGH treatment. Data in Table 3 show that BGH causes positive regression of the organ weight in the heart, pancreas, spleen, and ovaries, but not in other organs. It is clear that the somatotropic effect of BGH was not exerted equally to all organs, but differed from one to another. As in the case of hypophysectomized rats (Simpson *et al.*, 1949) both thymus and spleen were greatly enhanced by the growth-stimulating effect of BGH (Table 3).

As shown in Figure 1, a daily dose of 100 μg BGH is required to increase the body weight of the hypophysectomized hamster to the growth rate of normal control animals. Compared to hypophysectomized rats (Simpson *et al.*, 1949), the hypophysectomized hamsters appears to be equally sensitive to the growth-promoting action of BGH as evidenced by the increment of body weight and length.

There are no data in the literature to indicate that the weight of the pancreas is dependent on pituitary hormones. The present experiment clearly shows the growth-stimulating effect of BGH on the pancreas in the hamster (Table 3). It remains to be determined whether this effect is on the acinus cell or on the islets cells of the pancreas. Recently Gerhards and Ruhl (1974) and Curry *et al.* (1975) showed

that BGH counteracts the depressing effect of hypophysectomy on insulin secretion so that it returns to near or above normal levels in perfused hamster pancreases.

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References Cited

Becks, H., Asling, C. W., Simpson, M. E., Li, C. H., & Evans, H. M. 1949. "The growth of hypophysectomized female rats following chronic treatment with pure pituitary growth hormone. III. Skeletal changes: Tibia, metacarpal, costochondral junction and caudal vertebrae." *Growth* **13**, 175-189.

Bond, C. R. 1945. "The golden hamster (*Cricetus auratus*): Care, breeding and growth." *Physiol. Zool.* **18**, 52-59.

Breneneman, W. R. 1941. "Growth of the endocrine glands and viscera in the chick." *Endocrinology* **28**, 946-954.

Brody, S., & Ragsdale, A. C. 1922. "The equivalence of age in animals." *J. Gen. Physiol.* **5**, 205-214.

Curry, D. L., Bennett, L. L., & Li, C. H. 1975. "Dynamics of insulin release by perfused hamster (Mesocricetus auratus) pancreases: Effects of hypophysectomy, bovine and human growth hormone, and prolactin." *J. Endocrinol.* **65**, 245-251.

Freudenberger, C. B. 1932. "A comparison of the Wistar albino and the Long-Evans hybrid strain of the norway rat." *Amer. J. Anat.* **50**, 293-349.

Freudenberger, C. B. 1933. "Variability in body length, body weight and organ weights of the rat." *Anat. Rec.* **56**, 47-56.

Gerhards, E., & Ruhl, M. 1974. "Insulin secretion of the isolated perfused pancreas of the Chinese hamster (*Cricetulus griseus*)." *Acta Endocrinol.* **76**, 302-318.

Gilbreath, J. C., Jr., & Upp, C. W. 1952. "The growth pattern of a Cornish fowl." *Louisiana Agr. Expt. Stat. Bull.* **464**, 43 pp.

Li, C. H. 1954. "A simplified procedure for the isolation of hypophyseal growth hormone." *J. Biol. Chem.* **211**, 555-558.

Li, C. H., Simpson, M. E., & Evans, H. M. 1949. "The growth of hypophysectomized female rats following chronic treatment with pure pituitary growth hormone. II. Some chemical components of the musculature, liver and blood plasma." *Growth* **13**, 171-174.

Lostroh, A. J., & Li, C. H. 1958. "Effect of growth hormone and thyroxine on body weight of hypophysectomized C3H mice." *Endocrinology* **62**, 484-492.

MacDowell, E. C., Allen, E., & MacDowell, C. G. 1927. "The prenatal growth of the mouse." *J. Gen. Physiol.* **11**, 57-70.

MacDowell, E. C., Gates, W. H., & MacDowell, C. G. 1930. "The influence of the quantity of nutrition upon the growth of the suckling mouse." *J. Gen. Physiol.* **13**, 529-545.

McPhee, H. C., & Eaton, O. N. 1931. "Genetic growth differentiation in guinea pigs." *U.S. Dept. Agr. Tech. Bull.* **222**, 36 pp.

Ogle, C. 1934. "Climatic influence on the growth of the male albino mouse." *Amer. J. Physiol.* **107**, 635-640.

Poiley, S. M. in The Care and Breeding of Laboratory Animals, E. J. Farris, ed. 1950. J. Wiley and Sons Inc., New York, 142-143.

Simpson, M. E., Evans, H. M., & Li, C. H. 1949. "The growth of hypophysectomized female rats following chronic treatment with pure pituitary growth hormone. I. General growth and organ changes." *Growth* **13**, 151-170.

Smith, P. E. 1930. "Hypophysectomy and a replacement therapy in the rat." *Amer. J. Anat.* **45**, 205-273.

Webster, S. H., Liljegren, E. J., & Zimmer, D. J. 1947. "Body weight ratios for liver, kidneys, and spleen of laboratory animals." *Amer. J. Anat.* **81**, 477-513.

Webster, S. H., & Liljegren, E. J. 1949. 'Body weight ratios for certain organs of laboratory animals." *Amer. J. Anat.* **85**, 199-230.

Zucker, T. F., Hall, L., Young, M., & Zucker, L. 1941. "The growth curve of the albino rat in relation to diet." *Nutrition* **22**, 123-151.

Zucker, L., & Zucker, T. F. 1942. "A simple time weight relation observed in well nourished rats." *J. Gen. Physiol.* **25**, 445-463.