non-stressed animals and at this time there was also no significant cochlear trauma. Thus the increase in steroid secretion does not appear related to any anatomical cochlear changes. Rather it results from activation of neuroendocrine mechanisms involving the hypothalamic-pituitary-adrenal axis.

Summary. Rats were exposed to sound of 200-220 cps at an intensity of 130-135 db for 2, 12 or 48 hours. A marked increase in secretion of corticosterone was observed after 2 or 48 hours, and a marked decrease after 12 hours. Significant anatomical changes were not observed in the middle ears or cochleas of any of the animals. The data suggest that the changes in secretion rate of corticosterone do not depend on anatomical changes in the rat cochleas.

The author is deeply indebted to Dr. Drake W. Will for his assistance in interpreting the cochlear photomicrographs.

1. Frings, H., Frings, M., J. Acoust. Soc. Am., 1952, v24, 163.

2. Anthony, A., Ackerman, E., *ibid.*, 1955, v27, 1144.

3. Henkin, R. I., Knigge, K. M., Am. J. Physiol., 1963, v204, 710.

4. Knigge, K. M., Penrod, C., Schindler, W. J., *ibid.*, 1959, v196, 579.

5. Röhr, H., Beit. z. Anat., Physiol., u. Path. d. Ohres, d. Nase, u.d. Halses. 1921, v16, 14.

6. Marx, H., Z. f. Ohrenhk., 1909, v59, 333.

7. Kimura, M., Z. f. Hals-, Nasen-, und Ohrenhk., 1924, v8, 13.

8. Wever, E. G., Bray, C. W., Horton, G. P., Science, 1934, v80, 18.

9. Davis, H., Derbyshire, A. J., Kemp, E. H., Lurie, M. H., Upton, M., J. Gen. Psychol., 1935, v12, 251.

10. Kemp, E. H., Psychol. Bull., 1935, v32, 325.

11. Davis, H., Lurie, M. H., Hawkins, J. E., Comm. on Medical Res. of OSRD, 1943, v31, 1.

12. Wever, E. G., Smith, K. R., J. Exp. Psychol., 1944, v34, 239.

13. Smith, K. R., ibid., 1947, v37, 304.

14. Alexander, I. E., Githler, F. J., J. Comp. Physiol. Psychol., 1951, v44, 513.

15. —, *ibid.*, 1952, v45, 381.

16. Davis, H., WADC Tech. Rep. 53-58, March, 1953.

17. Smith, C. A., Covell, W. P., Eldredge, D. E., *ibid.*, 54-21, June, 1954.

18. Lurie, M. H., Davis, H., Hawkins, J. E., Jr., Laryng., 1944, v54, 375.

19. Covell, W. P., Rogers, J. B., *ibid.*, 1957, v57, 118.

20. ____, J. Comp. Neurol., 1953, v99, 43.

Received May 10, 1963. P.S.E.B.M., 1963, v113.

Fat-Mobilizing Effect of Growth Hormone in the Guinea Pig.* (28413)

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The rise in plasma free fatty acids (FFA) after parenteral administration of somatotropin preparations has been well-documented in several species tested with material from various sources(1-3). It is recognized that growth hormone preparations available are contaminated with small amounts of other pituitary principles; for brevity, the term somatotropin (or growth hormone) will be used in place of somatotropin preparation. This report concerns the response to an ovine (sheep) somatotropin in the guinea pig, a test animal heretofore not found responsive to several somatotropins (4).

Materials and methods. Male guinea pigs of mixed color, initial weight varying from 250-300 g, were used. Somatotropin used in these studies included ovine[‡] and bovine[§]

^{*} This investigation was supported by a Public Health Service training grant from Nat. Inst. of Arthritis and Metab. Dis.

[†] USPHS Research Fellcw, National Cancer Institute.

[‡]Kindly supplied by Endocrinology Study Section, Nat. Inst. of Health, N.I.H.-GH-S-4.

[§] Kindly supplied by Endocrinology Study Section, Nat. Inst. Health, N.I.H.-GH-B-2.

Exp	No. of animals	Test material	$\frac{\text{Mean FFA} \pm \text{S.D.}^*}{(\mu \text{eq/l})}$	% increase over control	P-value (vs control)
1	5	Control solution	1035 + 108	_	_
	5	Ovine G.H.	1818 ± 300	+75.7	<.001
	3	Bovine "	1260 ± 218	+21.7	>.1
	5	Human "	1304 ± 249	+26.0	>.05
2	5	Control solution	996 ± 121		—
	5	Ovine G.H.	1496 ± 136	+50.2	<.001

TABLE I. FFA Response to Various Somatotropins in the Guinea Pig.

* Mean FFA values 4 to 5 hr after injection of test material.

growth hormones, each prepared by potassium chloride-cold ethanol fractional purification(5), and human growth hormone, || obtained by the acetic acid extraction procedure(6). Assay of the sheep and beef preparations for other pituitary hormones was performed by the supplier, and in each case contamination was negligible. Prior to testing, the animals were fed guinea pig chow¶ and water ad lib. At the twelfth hour of a 16-hour fast, each guinea pig received a 1 ml intraperitoneal injection of either a control solution, ovine growth hormone (5 mg), bovine growth hormone (5 mg) or human growth hormone (2 mg). The lower dose of human somatotropin was based upon studies (7) indicating that human growth hormone has a much smaller molecular weight than bovine somatotropin, and also the effective dose of the human preparation in the dog and in the rat is smaller than of the bovine material. The diluent for each somatotropin preparation was the control solution: distilled water with sufficient 0.1 N NaOH added to dissolve the dry powder, to a final concentration of 5 mg growth hormone per ml (bovine and ovine) or 2 mg per ml (human). Between 4 and 5 hours after injection, the animals were stunned by a cervical blow, the abdomen was quickly incised, and a single blood sample taken from the abdominal aorta at the bifurcation. The blood was immediately transferred to oxalated tubes and gently inverted to assure anticoagulation. Plasma thus obtained was quickly frozen, and FFA levels were determined at a subsequent date by the method of Dole(8). Statistical evaluation was performed with the Student's t-test to calculate probabilities.

Results and discussion. The results of 2 experiments are summarized in Table I. In the first experiment, plasma FFA values 4 to 5 hours after administration of ovine somatotropin were significantly greater than after injection of the control solution, whereas those animals given either bovine or human growth hormone showed small increments in FFA of no statistical significance. The rise in FFA after ovine growth hormone injection was confirmed in a second experiment.

Somatotropin response, as measured by organ weight and total body weight, has not been observed in the guinea pig given bovine, simian, or even guinea pig growth hormone(4). Elevation of plasma FFA, regularly seen after administration of bovine, human or simian somatotropin to suitable species(1,2) has not previously been described in the guinea pig. Knobil(9) has stated that the hypophysectomized guinea pig exhibits "acute responses to a single injection of nonprimate hormone, such as a fall in the concentration of non-protein nitrogen and a rise in the level of non-esterified fatty acids in the plasma." The guinea pig was chosen as the test animal for ovine somatotropin to facilitate studies concerning the role of ascorbic acid in growth hormone responsiveness,** thereby obviating the necessity of producing clinical scurvy in man, monkey, the Indian fruit bat or the red-vented bulbul.

The author gratefully acknowledges the advice and criticism of Dr. Josiah Brown. The technical assistance of Miss Ruth Greene is greatly appreciated.

^{||} Kindly supplied by Dr. Josiah Brown, Raben lot #12.

[¶] Purina Chow, Ralston Co.

^{**} Now in progress.

1. Raben, M. S., Hollenberg, C. H., J. Clin. Invest., 1959, v38, 484.

2. Goodman, H. M., Knobil, E., Endocrinology, 1959, v65, 451.

3. Henneman, D. H., Henneman, P. H., J. Clin. Invest., 1960, v39, 1239.

4. Knobil, E., Greep, R. O., *Rec. Prog. Hormone Res.*, 1959, v15, 1.

5. Wilhelmi, A. E., in The Hypophyseal Growth

Hormone, Nature and Actions, Richmond Smith, Jr., ed., McGraw-Hill, New York, 1954, p59 ff.

6. Raben, M. S., Science, 1957, v125, 883.

7. ____, Rec. Prog. Hormone Res., 1959, v15, 71.

- 8. Dole, V. P., J. Clin. Invest., 1956, v35, 150.
- 9. Knobil, E., in Growth in Living Systems, M. X. Zarrow, ed., Basic Books, Inc., 1961, p358 ff.

Received February 19, 1963. P.S.E.B.M., 1963, v113.

Effect of Tetracycline on a Standardized Intracutaneous Staphylococcal Infection in Guinea Pigs.* (28414)

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During investigations into induced staphylococcal infections without concomitant disease it was found that tetracycline administration could recall a latent infection among guinea pigs if the initial infection had been induced with tetracycline resistant staphylococci. Tetracycline administration was followed by the anticipated changes in the indigenous microflora of the animals from predominantly gram-positive to predominantly gram-negative. It seemed possible, however, that tetracycline might influence the guinea pig-staphylococcal host parasite relationship in other ways.

Materials and methods. Mature, male guinea pigs were used. Nasal cultures obtained before and after crowding and tetracycline administration failed to reveal coagulase-positive staphylococci. One group of animals was then exposed to a tetracycline resistant staphylococcal aerosol. At least one month was allowed to pass before these animals were used for the present experiments. During this period the induced staphylococcal carrier state disappeared. The other group of animals was not exposed to the staphylococcal aerosol.

Two staphylococcal strains were used. Both were coagulase and mannitol positive, hemolytic, and resistant to penicillin G, streptomycin, and tetracycline. Strain 4974 is of phage type 80/81. Strain 5723 is of type 52A/79. The strains were grown in broth overnight, centrifuged and washed twice, and suspended in saline. The inocula consisted of 10^3 , 10^4 , 10^5 , 10^6 , and 10^7 viable units/0.1 ml, respectively.

Procedure. Forty-eight hours prior to infection, the hair over the dorso-lateral aspects of the animals was shaved and chemically depilated. Every effort was made to prevent breaking the skin.

The skin was prepared with 80% ethanol. The hairless areas were marked off in 3 cm squares, 3 to a side, on both sides. An additional site was prepared adjacent to the test sites on each side. A total of 8 test squares was therefore planned on each animal.

Six 0.1 ml intradermal injections of the bacterial inoculum were introduced into the test sites after preliminary preparation with 80% ethanol. One of the adjacent sites was injected with 0.1 ml of sterile saline, and one was left uninjected. Serial 10-fold dilutions of another 0.1 ml of each bacterial inoculum were made and plated in order to determine the infective charge.

Results. Untreated animals. No detectable lesion occurred when 10^3 or 10^4 viable units were injected (Table I). At 10^5 viable units there was usually a transient erythema with or without slight induration beginning at 24 hours after injection and lasting for an addi-

^{*} Supported by a grant from Nat. Inst. of Allergy and Infect. Diseases, Nat. Inst. Health, U.S.P.H.S.