noted in C57 Black mice receiving pretreatment with glucose 20 minutes before 1.0 mg goldthioglucose per gram body weight was administered.

Discussion. The results of these experiments show that administration of goldthioglucose, in amounts that have been shown to induce obesity(4), causes destruction in widely scattered areas of the brain. They are not limited to the ventromedial nucleus nor even the ventromedial region of the hypothalamus. The functions of many of the damaged nuclei, as classically defined, are rather remote from the function of regulating food intake. Damage to nuclei in the vicinity of the area postrema may occur at levels of goldthioglucose administration far below that requisite for hyperphagia and ensuing weight gain. Finally, it appears noteworthy that sites in the brain damaged by parenterally administered goldthioglucose have in common proximity to loci where the blood-brain barrier has been demonstrated to be deficient to trypan blue, to silver nitrate administered in drinking water(5), and to radioactive isotopes(6). Recent work using labeled goldthioglucose(7) demonstrated radioactivity in the hind brain as well as in the hypothalamus.

Conclusion. Goldthioglucose administration to inbred C57 Black and CBA mice, in amounts sufficient to induce hyperphagia and massive weight gain, results in lesions of nuclei adjacent to the area postrema of the medulla oblongata, to the median eminence of the hypothalamus, to the supraoptic crest between the hypothalamus and the basal telencephalon, and between the subcommissural and subfornical organs associated with the midbrain-epithalamic transition and the hippocampal formation. The hypothesis is advanced that the observed distribution of the lesions is related to deficiency of the blood-brain barrier at these sites.

1. Mayer, J., *Metabolism,* 1957, v6, 435.
2. Larsson, S., *Acta Physiol. Scand.,* 1957, v40, 367.
3. Marshall, N. B., Barrnett, R. J., Mayer, J., PROC. SOC. EXP. BIOL. AND MED., 1955, v90, 240.
4. Liebelt, R. A., Perry, J. H., *ibid.,* 1957, v95, 774.
5. Wislocki, G. B., Ledue, E. H., *J. Comp. Neur.,* 1952, v96, 371.
6. Bakay, L., *The blood-brain barrier.* Chas. C Thomas, Springfield, 1956.
7. Swartz, H. A., Christian, J. E., Andrews, F. N., *Am. J. Physiol.,* 1960, v199, 67.

Received October 10, 1960. P.S.E.B.M., 1961, v106.

Effect of Synthetic Steroid or Phenanthrene Compounds upon Weight Gain and Feed Efficiency of Rats.* (26237)

E. W. HARTSOOK AND T. V. HERSHBERGER (Introduced by N. B. Guerrant)
Department of Animal Industry and Nutrition, Pennsylvania State University, University Park

Previous work has shown that estrogens tend to increase rate of gain and efficiency of feed utilization in ruminant animals(1,2), but generally depress these responses in non-ruminant animals(3-5). Evidence has appeared in the literature(6,7) to indicate that modification of estrogenic compounds by oxidation reactions yields substances which are non-estrogenic and therefore have reduced inhibitory effect on non-ruminant growth, but nevertheless retain the properties of their parent substances in inducing pituitary release of trophic factors.

Randall and Selitto(8) indicated that the compound Ro - 2 - 7239 (2 - acetyl - 7 - oxo - 1,2,4,4a,4b,5,6,7,9,10,10a - dodecahydrophenanthrene) administered subcutaneously for 7 days at a rate of .5 mg/rat/day exhibited a tendency to increase the gain of female rats. It was of interest to investigate the effect of feeding this compound at somewhat lower levels upon body weight gain and feed efficiency in female rats and in nor-

* Authorized on April 4, 1960 for publication as paper No. 2458 in Journal Series of Penn. Agric. Exp. Station.

TABLE I.

Item and animal	Diet 1, basal*	Diet 2, SC-6582	Diet 3, Ro-2-7239	S.E. of means†	L.S.D.‡
A. Effect of SC-6582 or Ro-2-7239 on wt gain and feed efficiency of adult rats					
1. Wt gain (g/28 days)					
Normal male	71.7 §¶	69.9 ¶	57.8 **	±6.0	11.3
Castrate "	70.0 ¶	61.8	65.6 ‖		
Normal female	57.4	52.9	52.0		
2. Feed efficiency (g gain/g feed)					
Normal male	.180‖	.175¶	.145**	± .012	.028
Castrate "	.176‖	.154	.164‖		
Normal female	.144	.132	.130		
B. Effect of SC-6582 or Ro-2-7239 on pituitary, thyroid and adrenal tissue/100 g of body wt of adult rats					
3. Pituitary (mg/100 g)					
Normal male	3.36§	3.02	3.08	± .28	.79
Castrate "	4.84	5.03¶	5.06¶		
Normal female	4.72	4.23¶	4.18¶		
4. Thyroid (mg/100 g)					
Normal male	4.90	5.43	5.70	± .48	1.42
Castrate "	6.04	6.10	5.96		
Normal female	6.98¶	6.82	6.30		
5. Adrenals (mg/100 g)					
Normal male	15.35	15.31	18.77	±1.36	4.41
Castrate "	18.24	17.09	20.74		
Normal female	27.13¶	28.43¶	24.60‖		
C. Effect of SC-6582 or Ro-2-7239 on testes or uterus/100 g of body wt of adult rats					
6. Testes (g/100 g), normal ♂	1.13§	1.28	1.36	±.11	.35
7. Uterus (g/100 g), normal ♀	.16	.12	.11	±.03	.13

* Rockland rat diet.
† Pooled stand. error of means.
‡ Least difference between means required for significance at 5% probability level.
§ Mean of 4 observations.
‖ Significant at $P < .05$.
¶ Significant at $P < .01$. [These symbols (‖,¶) used to compare the greater responses to the smallest response for each experimental diet.]
** Significant at $P < .05$. [This symbol (**) used to compare responses to experimental diets with that to basal diet for each class of animals.]

mal and castrate male rats under the condition of controlled equalized feed intake.

Cook *et al.*(9) indicated that subcutaneous injection of approximately 5 mg or more of compound SC - 6582 (17*α* - methyl - 17 - hydroxy - 5(10) - estren - 3 - one)/kg of body weight increased the rate of weight gain of cholesterol-fed cockerels. Subcutaneous injection of 1-5 mg of this compound/rat/week appeared to decrease body weight gain of castrate immature male rats. It was of interest to compare the effect of feeding this compound at somewhat lower levels to castrate male, as well as normal male and female rats under the condition of equalized feed intakes.

The present work involved feeding compounds Ro-2-7239 or SC-6582 under conditions of equalized and *ad libitum* feeding to normal female and normal and castrate male albino rats. The criteria evaluated were body weight gain and feed efficiency. Weights of pituitary, thyroid, adrenal, and testes or uterus were also observed.

Materials and methods. Experiment 1: Twenty-four male and 12 female young adult Wistar rats were used. Twelve of the males were castrated under ether anesthesia 1 week prior to initiation of the feeding experiment. The animals were allotted as 4 replicates of 9 animals each in a 3 x 3 factorial design to 3 experimental diets and amount of feed offered within each replicate was limited to that of the animal consuming the least. Tap

TABLE II. Effect of SC-6582 or Ro-2-7239 on Weight Gain, Feed Efficiency, and Organ Weight of Young Rats.

Item and animal	Treatment means							S.E. of means*	L.S.D.†
		SC-6582			Ro-2-7239				
	Basal diet	.75 μg	1.5 μg	3.0 μg	.75 μg	1.5 μg	3.0 μg		
1. Wt gain (g)									
Normal male (25 days)	169.0	152.5	165.0	165.2	171.0	157.2	158.8	± 6.5	19.3
" female (28 days)	126.5	106.0	115.0	120.2	113.5	115.0	126.0	±11.9	39.7
2. Feed efficiency (g gain/g feed)									
Normal male	.380	.365	.370	.370	.382	.359‡	.359‡	± .008	.02
" female	.290	.272	.263	.279	.274	.266	.290	± .029	.10
3. Pituitary (mg/100 g)									
Normal male	3.43	3.57	3.62	3.38	3.52	3.67	3.34	± .16	.47
" female	4.76	4.68	5.07	5.09	4.92	5.01	4.36	± .55	1.85
4. Thyroid (mg/100 g)									
Normal male	5.69	5.78	6.53	6.24	5.26	5.48	6.60	± .42	1.21
" female	6.68	6.44	7.12	7.34	6.60	7.16	6.62	± .61	2.05
5. Adrenals (mg/100 g)									
Normal male	14.64	15.31	15.45	17.42§	14.62	15.44	15.12	± .64	1.93
" female	26.28	27.66	28.06	26.21	31.20	29.72	25.58	± 2.44	8.14
6. Testes (g/100 g)	.96	.93	1.04	.83	1.04	1.12	1.02	± .10	.30
7. Uterus (g/100 g)	.15	.22	.15	.12	.16	.21	.10	± .03	.11

* Stand. error of means.
† Least differences required for significance at 5% probability level.
‡ Significant at P = <.05.
§ " P = <.01.

water was given *ad libitum*. Diet 1 (basal) was a ground rat diet,† diets 2 and 3 were the basal diet with additions of 1 μg of SC-6582‡ and Ro-2-7239,‡ respectively, per g of diet. At the end of 43 days (Replicates 1 and 4) or 37 days (Replicates 2 and 3) on experiment the animals were killed with chloroform, and pituitary, thyroid and adrenals were excised from all animals as were testes or uterus from appropriate animals.

Experiment 2: Forty-two Wistar rats (28

†Rockland rat diet, A. E. Staley Mfg. Co., Decatur, Ill.

‡ Premixes of compounds SC-6582 or Ro-2-7239 were made by mixing 0.1 g with 99.9 g cerelose. Sufficient cerelose was added to the basal diet to equal that of the premix added to experimental diets. The authors wish to thank Dr. D. L. Cook, G. D. Searle & Co., Chicago, Ill. and Dr. L. O. Randall, Hoffman-LaRoche Inc., Nutley, N. J., respectively, for generously making available supplies of compounds SC-6582 and Ro-2-7239.

males, 34-73 g, and 14 females, 39-79 g) were randomly allocated to treatments involving *ad libitum* feeding of 7 experimental diets. Diet 1 (basal) was a ground rat diet,† diets 4-6 were a ground rat diet containing .75, 1.5 and 3.0 μg, respectively, of SC-6582‡ per g of diet, and diets 7-9 were a ground rat diet containing .75, 1.5 and 3.0 μg, respectively, of Ro-2-7239‡ per gram of diet. Tap water was given *ad libitum*.

Statistical comparison of treatment means was done by using error mean squares, obtained from analyses of variance, to compute least differences required for significance (10).

Results. Data obtained by feeding normal and castrate male rats and normal female rats equal quantities of compounds SC-6582 or Ro-2-7239 are shown in Table I. Results of feeding, individually to appetite, normal male or female rats graded levels of the compounds SC-6582 and Ro-2-7239 are shown in Table II.

Our experiments show that both compounds tend to depress gain and feed efficiency. The depression of these responses reached significant levels in the case of compound Ro-2-7239 fed to normal male rats at the 1 μg/g level employed in Exp. 1. No significant changes in size of pituitary or thyroid glands were observed upon feeding of either compound. Compound SC-6582 at the 3 μg/g level significantly increased the size of adrenals of normal male rats. No significant changes in size of testes or of uterus were noted in the case of either compound.

Discussion. Administration of compound SC-6582 did not produce an increase in uterine weight/100 g of body weight, a finding at variance with the cited work(9). A considerably smaller total amount of substance administered in the present work may explain the lack of agreement.

Administration of compound Ro-2-7239 tended to reduce, or leave unchanged, the size of adrenals of female rats. This finding agrees with that of the previous work(8), but the tendency to increased size of these glands in normal and castrate male rats is interesting. A tendency toward increased size of testes was also found with this compound and agrees with the results of the previously cited work.

Summary. Studies have been made of the effects of feeding 2 compounds, Ro-2-7239 (2-acetyl - 7 - oxo - 1,2,4,4a,4b,5,6,7,9,10,10a - dodecahydrophenanthrene) or SC - 6582 (17α - methyl - 17 - hydroxy - 5(10) - estren-3-one), to rats at levels of .75, 1.0, 1.5, or 3.0 μg/g of diet. Equalized or *ad libitum* feeding was employed with weanling or young adult normal or castrate males or normal females. Compound Ro-2-7239, but not compound SC-6582, significantly inhibited both weight gain and feed efficiency in normal male rats. No significant changes in response to either compound were noted in castrate males or normal females. Compound SC-6582 at the 3 μg/g level, but not compound Ro-2-7239, produced significant increases in size of adrenals in normal male rats. Neither compound at the 3 μg/g level produced significant alteration in size of pituitary, thyroid, testes, or of uterus.

1. Burroughs, W., Culbertson, C. C., Kastelic, J., Cheng, E., Hale, W. H., *Science,* 1954, v120, 66.

2. Hale, W. H., Homeyer, P. G., Culbertson, C. C., Burroughs, W., *J. Animal Sci.,* 1955, v14, 909.

3. Sykes, J. F., Andrews, F. N., Hill, F. W., Lorenz, F. W., Thomas, J. W., Winchester, C. F., *Nat. Research Council Pub. No. 266,* 1953.

4. Hartsook, E. W., Magruder, N. D., *Am. J. Physiol.,* 1957, v190, 255.

5. Sewell, R. F., Warren, E. P., O'Mary, C. C., *J. Animal Sci.,* 1957, v16, 20.

6. Smith, O. W., Vanderlinde, R. E., *Endocrinology,* 1951, v49, 742.

7. Vanderlinde, R. E., Vasington, F. D., Westerfeld, W. W., *J. Am. Chem. Soc.,* 1955, v77, 4176.

8. Randall, L. O., Selitto, J. J., *Endocrinology,* 1958, v62, 693.

9. Cook, D. L., Edgren, R. A., Saunders, F. J., *ibid.,* 1958, v62, 798.

10. Snedecor, G. W., *Statistical Methods Applied to Experiments in Agriculture and Biology,* 4th ed., Ames, Iowa State College Press, 1946, p406.

Received October 10, 1960. P.S.E.B.M., 1961, v106.