

10471

Effect of Brief Experimental Hyperthyroidism on Reproduction in the Rat.

C. P. KRAATZ. (Introduced by L. B. Nice.)

From the Department of Physiology, Chicago Medical School.

The experiment here reported endeavors to determine whether a short, vigorous treatment with thyroid substance will stimulate ovarian function in the rat, without the marked disturbance of reproduction observed after lengthy treatment.^{1, 2, 3}

Thyroid substance (Wilson) mixed with a few drops of water was fed by medicine dropper to 35 virgin female rats (Sprague-Dawley strain) 4 to 6 months old. Daily dosages of 0.25 and 0.3 g per rat were given for periods of 3, 4, and 5 days. Animals were allowed to mate with normal males at the first estrous period after the last feeding. Thirty-five untreated littermates served as controls. The data on reproduction in the latter throughout the year approximate the figures for the local and parent colonies.⁴

The experimental animals fall into 2 groups, Series A, treated in June, and Series B, treated in April, October, and December. Results are summarized in Table I.

Series A typifies the more pronounced effect of thyroid administration observed during hot weather: the loss of body weight is greater

TABLE I.
Breeding Experiments with Thyroid-fed Female Rats and Littermate Controls.

	Series A	Series A Controls	Series B	Series B Controls
Animals exposed to males	9	6	26	29
Total litters resulting	8	6	26	24
Avg preliminary wt of mothers, g	218.1	230.2	219.6	215.5
'' loss of wt. on thyroid, %	8.1	—	5.8	—
'' No. of young per litter	8.25	10.0	12.3	9.0
'' wt of young at birth, g	5.78	5.6	5.36	5.92
'' age at eruption of upper incisors, days	7.6	8.0	8.5	8.1
% of young living 21 days*	51.1	91.6	71.8	69.4
Avg wt of young at 21 days of age, g (determined only on litters of 6)	36.8	42.2	37.5	37.8

Series A—fed thyroid during June, 1938.

Series B—fed thyroid during April, October and December, 1938.

*Litters reduced to 6 at an early age.

¹ Gudernatsch, J. F., *Am. J. Physiol.*, 1915, **36**, 370.

² Hayashi, H. H., *Bull. de l'Acad. de Méd.*, 1929, **101**, 115.

³ Weichert, C. K., *Physiol. Zool.*, 1930, **3**, 461.

⁴ Personal communication from Evan C. Holtzman of Sprague-Dawley, Inc.

than that of Series B on the same dosage. The somewhat smaller litters and markedly reduced survival of the young in Series A suggest the reproductive disturbances of severely hyperthyroid animals.

Series B, on the other hand, shows a stimulation from thyroid treatment during cooler weather. The litter size is definitely higher than in the controls, accompanied by a slightly lower weight of the young at birth. Survival in Series B, though low, is the same as in the controls and development proceeds at an essentially normal rate as evidenced by the figures on tooth eruption and 21-day weight. Litters were reduced to 6 within 3 or 4 days after birth so comparison of the figures is justifiable.

The frequency distribution of all litters according to size is shown in Fig. 1.

Six of the 26 litters in Series B are larger than the maximum control litters with only 3 falling below the control average of 9.2, while only 3 of the 30 control litters are larger than the 12.3 average of Series B.

As mentioned, an attempt was made to induce conception as early as possible after thyroid treatment. Table II lists the litters of Series B according to the interval between the end of thyroid administration and fertilization.

DISTRIBUTION OF LITTERS ACCORDING TO SIZE

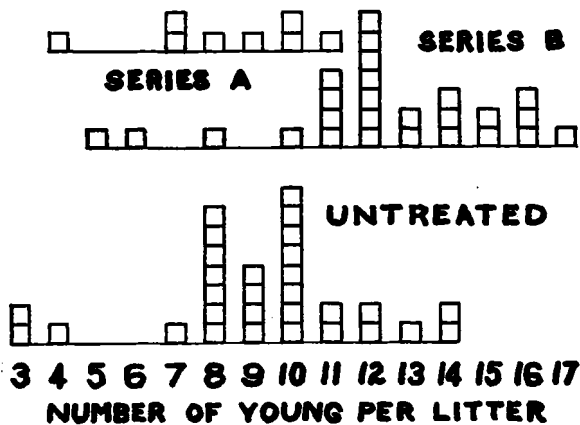


FIG. 1.

Frequency distribution of all litters. Series A received thyroid treatment in June, Series B in April, October and December. Untreated animals from both series are combined.

TABLE II.
Distribution of Series B Litters Relative to Thyroid-feeding Period.

	Day sperm was found in the vaginal smear; "0" is the last day of feeding							
	0	1	2	3	4	5	6	22
No. of young in litter	6	11 12 12 13 14 15 15	11 11 14 16 16 17 15	8 10 12 12 13 13 16	12 14		5 11	12
Avg litter size		13.1	14.2	11.9	13.0		8.0	

The first 4 days following thyroid feeding appear to be an "effective period," for the 22 rats bred during days 1 to 4 delivered an average of 13.0 young per mother. The present experiment, however, does not necessarily determine the extent of this period.

The range of dosages used varied little in its effects, except possibly with the highest dose. Of the 22 rats fertilized during the effective period, 2 receiving 0.3 g of thyroid daily for 3 days averaged 12.0 per litter; 7 receiving 0.3 g for 4 days averaged 12.4; 8 receiving 0.25 g for 5 days averaged 12.6, and 5 receiving 0.3 for 5 days averaged 14.8.

Of another series of 8 animals receiving 0.4 g of thyroid daily for 10 days, only 3 delivered litters (15, 8, and 5 young) and 2 of these failed to nurse them.

Kunde, Carlson and Proud⁵ record an observation suggestive of the results reported here. In rabbits under continued thyroid treatment begun before mating, they found at laparotomy early in pregnancy an abnormally high number of fetuses, although few were born alive.

An augmented liberation of ova may or may not be a factor in the increased litter size following limited thyroid treatment. That the number of ova is the determining factor in litter size seems improbable in the light of the report of Long and Evans⁶ that they found an average of 9.6 ova in the tubes of their rats, while the average litter size of the colony was 6.9. The strain of rats used in the present experiment, averaging 9 per litter, may conceivably liberate an average of 13 ova.

A tentative and partial explanation better supported by the available evidence is that the hyperthyroidism stimulates the release of luteinizing hormone from the anterior pituitary. The consequent

⁵ Kunde, M. M., Carlson, A. J., and Proud, T., *Am. J. Physiol.*, 1929, **88**, 747.

⁶ Long, J. A., and Evans, H. M., *Memoirs of the Univ. of Cal.*, 1922, v. 6.

increase in secretion by the ovary provides for the maintenance in the uterus of a higher number of embryos. Van Horn⁷ found that the gonad-stimulating power of the hypophysis was increased in female rats hyperthyroid for several weeks. Halpern and Hendryson,⁸ after brief daily treatment of non-pregnant adult rats with 0.5 g of thyroid, observed enlarged ovaries with increased corpus luteum development and suggested an activation of the "lutein-stimulating" hormone of the anterior pituitary. Hayashi² made similar observations with a lower dosage and described degeneration of the corpora lutea under long treatment.

Summary. The daily administration of 0.25 to 0.3 g of thyroid substance to adult female rats for 3 to 5 days during April, October and December, followed by mating within 4 days to normal males, resulted in an average litter size of 13.0, as compared to 9.0 in untreated littermates. Similar treatment during hot weather or an increase in thyroid amount proved deleterious to reproduction.

10472 P

Significance of Sex Hormones in Tanning of the Skin of Women.

JAMES B. HAMILTON.* (Introduced by Edgar Allen.)

From the Department of Anatomy, Yale University School of Medicine.

As illustrated in castrated and eunuchoid men, tanning of the human skin is abetted by the presence and negated by the absence of effective levels of male hormone substances in the body tissues and fluids.¹ Pending completion of analyses of urinary hormone titers and spectrophotometric study of skin pigmentation, the present report will serve to indicate that both the tanning process and its dependence on hormones for photograph-like "development" are (a) somewhat similar in women to those described for men, (b) capable of induction in women by male hormone substance, and (c) influenced by female as well as by male hormones.

⁷ Van Horn, W. M., *Endocr.*, 1933, **17**, 152.

⁸ Halpern, S. R., and Hendryson, I. E., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **33**, 263.

* This investigation was supported in part by a grant from the International Cancer Research Foundation.

¹ Hamilton, James B., and Hubert, Gilbert, *Science*, 1938, **88**, 481.