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Effect of Ovariectomy and Replacement Therapy Upon Thyroxine Secretion Rate of Rat.* (25414)

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The role of ovarian hormones in influencing thyroid function has been the subject of many investigations. It has been reported that ovariectomy depresses(1,2) or has no effect upon thyroid function(3,4). Moreover, estrogen administration may increase(5,6,7), decrease(8,9), or exert little effect(3) upon thyroid activity depending upon dose and length of treatment. Progesterone, on the other hand, increased thyroid function(5,10) but when administered concomitantly with estrogen, a depressing effect has been reported (11). In the above studies various indices of thyroid activity have been used, such as release of thyroidal-I^{131}, I^{131} uptake, thyroid histology and cytology and hyperplasia. Since there is little agreement concerning the problem, it seemed desirable to determine quantitatively the influence of ovariectomy upon thyroxine secretion rate (TSR) at various periods postcastration and effect of ovarian hormone replacement therapy.

Materials and methods. Young mature female rats of Sprague-Dawley-Rolfsmeyer strain with initial weight of 190-230 g were housed at uniform temperature of 78 ± 1°F in a room artificially illuminated during normal daylight hours. They were given Purina Lab Chow and fresh water daily. Each rat was injected i.p. with 2 μc carrier-free I^{131}. Forty-eight hours were allowed for I^{131} fixation by the thyroid. External neck counts were taken at this time and every 48 hours thereafter by first anesthetizing each animal with ether, then placing it on a lead plate with neck resting on a scintillation probe containing a 2″ NaI crystal. Care was taken in placement of animal to insure same geometrical relationship at each successive counting period. Thyroidal radioactivity was measured with scintillation counter, Nuclear-Chicago (N.C.) Model DS5, connected to rate meter, N.C. Model 1620 A. Conventional corrections were made for decay of isotope and background. *Determination of thyroxine secretion rate (TSR).* Each rat was injected subc. with .5 μg/100 g l-thyroxine for 2 consecutive days beginning 4 days after I^{131} injection, in such manner that ovariectomized rats received initial thyroxine injection either on day of ovariectomy or at days 6, 20, 70, and 84 postcastration. Thyroxine dose was increased at .5 μg/100 g increments, each dose injected for 2 consecutive days, with neck counts made on day of each increase. TSR was determined by plotting the percent previous count with thyroxine dose. The dose which prevented further thyroidal-I^{131} output in each rat (95-100% previous count) was estimated as its TSR. Some ovariectomized rats received daily subc. injections of 1 μg estradiol benzoate (EB) and/or 3 mg progesterone (P), commencing day of initial thyroxine injection and continuing until their TSR was established. Intact rats of same age and body weight range served as controls for each series of TSR determinations.

Results. Effect of ovariectomy and replacement with EB and/or P upon average daily thyroxine secretion rate (TSR) is pre-

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TABLE I. Effect of Ovariectomy and Estradiol Benzoate (EB) and/or Progesterone (P) Replacement upon Thyroxine Secretion Rate in Rats.

Treatment	No. of rats	Avg Body wt, g	Avg TSR, μg l-thyroxine/100 g/day	Probability
Series I				
Intact	18	217.4	1.08 ± .06‡	
Ovariectomized (2-6)*	16	223.0	.72 ± .06	.01
Series II				
Intact	41	239.9	1.09 ± .08	
Ovariectomized (8-12)	16	244.2	.63 ± .07	.01
" (22-28)	17	253.8	.70 ± .09	.02
Series III				
Intact	10	265.0	1.10 ± .16	
Ovariectomized (72-74)	11	304.1	.64 ± .10	.05
" (86-90)	13	308.9	.62 ± .06	.01
Series IV†				
Intact	12	244.5	1.20 ± .16	
Ovariectomized + 1 μg EB (2-8)	12	227.1	1.13 ± .11	
Idem + 3 mg P (2-8)	12	224.9	1.17 ± .09	
Ovariectomized + 3 mg P (2-6)	15	255.0	.73 ± .11	.02
Aggregate				
Intact	81		1.11 ± .05	
Ovariectomized	73		.66 ± .03	.001

* Denotes days ovariectomized before TSR was established.
† Initial EB and/or P inj. on day of ovariectomy.
‡ Stand. error of mean.

sented in Table I. TSR of ovariectomized rats determined immediately postcastration (2-6 days) was .72 μg/100 g l-thyroxine. This represented a decrease of approximately 33% when compared with intact controls of same age and body weight range. Increasing the period of ovariectomy to approximately 3 months did not produce any further significant lowering of TSR. Differences in TSR between respective age controls were also insignificant. Ovariectomized rats receiving 1 μg EB alone and with 3 mg P exhibited TSR's (1.13 and 1.17, respectively) in range of intact controls. Administration of 3 mg P alone did not significantly alter the decrease in TSR which resulted upon ovariectomy.

Discussion. Several investigators have attempted to define the relationship between ovarian and thyroid function. Contradictory results in previous studies(1,3,5,7) may be due to lack of sensitivity of methods employed for measuring thyroid activity. Our investigation, however, clearly indicates a reduction in thyroid function following ovariectomy since TSR was reduced approximately 33% as compared with intact controls. It also appears that reduction in thyroid function occurs in a relatively short period of time, since no further decrease in TSR was evident in rats ovariectomized 80 days or more. Although the mechanism by which ovariectomy reduced thyroid activity is not clear, the data from injection of 1 μg EB alone, and with 3 mg P appear to implicate a diminution in circulating estrogen level as a contributing factor since TSR of ovariectomized rats receiving estrogen was maintained at control level, whereas injection of P alone had little or no effect in maintaining TSR. It has been shown that a single injection of 1 μg EB increases 6 hour I^{131} uptake in ovariectomized rats, but has no effect in hypophysectomized-ovariectomized animals(5). This suggests that estrogen may stimulate increased secretion of thyrotropin (TSH) by adenohypophysis and a subsequent increase in I^{131} uptake by the thyroid. More recent studies(7, 12, 13) indicate large doses of estrogen, administered for prolonged periods of time, may stimulate thyroid directly. It is likely, however, that ovariectomy results in a lower circulating estrogen level and this, in turn, may

reduce TSH secretion and a subsequent reduction in thyroid activity. Such an interpretation appears consistent with observations that a physiological level of estrogen prevents reduction in TSR following ovariectomy and only increases thyroid activity if the adenohypophysis is intact(5).

Summary. 1) Effect of ovariectomy and replacement with 1 μg estradiol benzoate (EB) and/or 3 mg progesterone (P) upon daily thyroxine secretion rate (TSR) has been studied in mature rats. 2) Ovariectomy reduces TSR approximately 33% within 2-6 days postcastration. Increasing the interval to approximately 90 days between ovariectomy and TSR determination did not result in a further reduction in TSR. EB alone and with P prevented decrease in TSR following ovariectomy but P alone had no effect. 3) It is suggested that ovariectomy reduces the circulating estrogen level which, in turn, may reduce thyrotropin secretion and, subsequently, lower daily TSR.

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Effects of Age, Sex and Line on Serum Alkaline Phosphatase of the Chicken.* (25415)

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Serum alkaline phosphatase has been studied to some extent in the chicken. Its level has been reported to be higher in the young chicken than in the adult(1,2), and higher in the laying hen than in the adult male(1,3,4). Gutowska *et al.*(5) reported serum alkaline phosphatase in high producing hens to be higher than that of poor producing ones. However, other workers(1,6) reported that it bears no relation to rate of egg production. Several workers(1,4,6) have observed no significant difference between the phosphatase values of laying and those of non-laying females. A high line for serum alkaline phosphatase has recently been developed by selection based on activity of the enzyme measured at 6 weeks of age in a random bred population of White Leghorn chickens (Wilcox and Shaffner, unpublished). The present study was conducted to determine to what extent, if any, the high line differs from its random bred control at other ages. This might in turn also provide information as to the physiological nature of genetic modification in the activity of this enzyme. The present work was undertaken also to elucidate the effects of age and sex on serum alkaline phosphatase in the chicken.

Materials and methods. Males and females of a high serum alkaline phosphatase line and a random control line of White Leghorn chickens were used. The birds were fed *ad libitum*. Blood was taken at different ages from 10 males and 10 females randomly selected from

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