period of 2-2½ minutes to account for the plasma clearance curves of Fig. 2 solely on the basis of redistribution. This rapid rate of clearance, even after the inhibition of amine-metabolizing enzymes, is compatible with the observation that circulating catecholamines are taken up quickly by many tissues of the body(3,6).

Summary. The simultaneous inhibition of catechol-O-methyl transferase and monoamine oxidase (by pyrogallol and JB-835) produced only moderate prolongation of the cardiovascular effects of injected *l*-norepinephrine in anesthetized dogs. This prolongation of pharmacological action in presence of enzyme inhibitors was correlated with a delayed disappearance of injected norepinephrine from the circulation. While these results indicate that metabolism by these enzymes contributes to removal of circulating norepinephrine from the plasma in the dog, they further suggest that the physiological inactivation of circulating norepinephrine at the receptor sites does not require metabolic destruction of the amine by these enzymes.

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Thyroid: Serum Radioiodide Concentration Ratio During the Estrous Cycle of the Mouse.* (26973)

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The thyroid gland is known to exhibit variations in its activity which are closely correlated with changes in the estrous cycle. The thyroid concentrates more iodide during late estrus in rats(1) and in estrus in rabbits(2). However, in mice it has been reported to be more active during proestrus(3). Because of this apparent species difference it was of interest to reinvestigate thyroid activity in cycling mice. In this investigation thyroid: serum radioiodide concentration ratios (T/S) were determined simultaneously with the identification of the stage of the cycle. This measurement is much less influenced by factors outside the pituitary-thyroid axis than is percentage uptake of I^{131} as has been used by previous investigators. Also, these workers have determined uptakes on the basis of 4 stages of the estrous cycle; it was felt that by subdividing the cycle into 6 stages, more precise information could be obtained concerning the relationship between thyroid function and the reproductive cycle of mice.

Material and methods. Adult Swiss Webster mice weighing between 25 and 30 g were used in this experiment. All were fed Rockland laboratory chow *ad libitum* for at least one week before measurement of the T/S.

To determine T/S, 1 mg of propylthiouracil (PTU) in 0.25 ml of alkaline solution was injected subcutaneously 45 minutes before a subcutaneous injection of 1 μc of carrier-free I^{131} in 0.25 ml of distilled water. One hour later, the animals were anesthetized with ether and blood was obtained from the abdominal aorta. The thyroid was dissected out and weighed on a Roller-Smith torsion balance. One-tenth ml of serum and the thyroid were prepared for radioactivity determination by the method described by VanderLaan and Greer(4).

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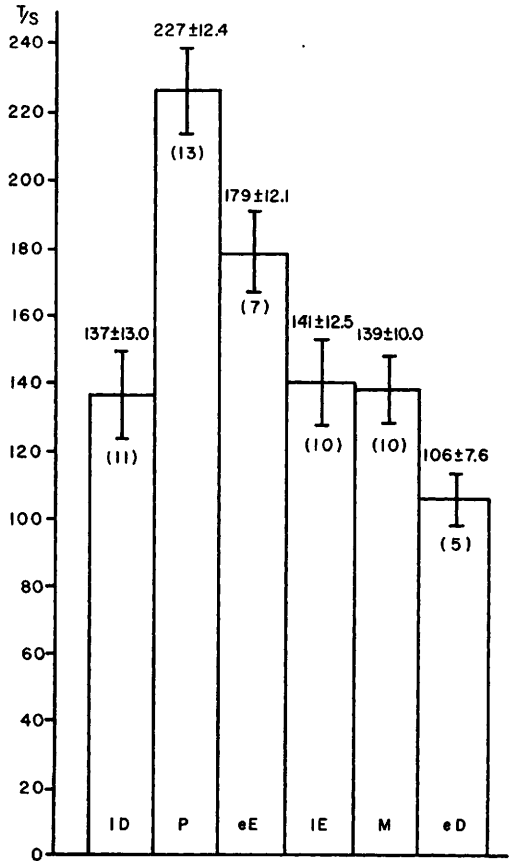

FIG. 1. Thyroid : serum radioiodide concentration ratios (T/S) during the various stages of the estrous cycle. Vertical bars represent mean T/S values, vertical lines standard errors of means. Figures within bars represent number of mice in group. (P = proestrus, eE = early estrus, lE = late estrus, M = metestrus, eD = first half of diestrus, lD = second half of diestrus).

P values:

P vs eE	.05-.02	eE vs lE	.05	lE vs eD	n.s.
P vs lE	<.01	eE vs M	.05-.02	lE vs lD	n.s.
P vs M	<.01	eE vs eD	<.01	M vs eD	<.05
P vs eD	<.01	eE vs lD	.05-.02	M vs lD	n.s.
P vs lD	<.01	lE vs M	n.s.	eD vs lD	n.s.

Vaginal smears were taken for 5 or more days and only animals that were cycling were used. Since the diestrus interval is commonly the longest interval and the most variable, we found it convenient to divide it into a first and second half. First half of diestrus was considered to be the day following metestrus, whereas the second half was the second day of diestrus. On the day of the experiment vaginal smears were performed approximately one to 5 minutes before the animal was sacrificed. Only those mice whose vaginal smears could be identified unequivocally as typical of one of the 5 stages of the estrous cycle (proestrus, early estrus, late estrus, metestrus, and diestrus) were used in the experiment.

Results. As shown in Fig. 1, the thyroid: serum radioiodide concentration ratio was found to be highest during proestrus. This value was significantly different from all other stages. With the onset of early estrus T/S decreased, reaching its lowest level in the first half of diestrus. T/S ratios of late estrus, metestrus, and second half of diestrus were essentially alike and not significantly different from the values found during the first half of diestrus.

Discussion. Our results confirm the finding of Soliman and Reineke(3) that in cycling mice the maximum uptake of radioactive iodide is obtained during proestrus. However, by dividing the estrous cycle into 6 stages, we were able to demonstrate that the thyroid also concentrates a significantly greater amount of radioiodide during early estrus than during the other stages of the cycle. Furthermore, we did not find an increased incorporation of radioiodide in diestrus as did Soliman and Reineke(3). In fact, the first half of diestrus was found to be the least active and the second half of diestrus was essentially the same as late estrus and metestrus. The explanation for the difference between the 2 findings may be due to their determining uptakes 6 hours after identification of the stage of the estrous cycle. It is conceivable that some of the animals were actually in proestrus at time of sacrifice, which then resulted in finding false high values for the diestrous period.

The thyroid:serum radioiodide concentration ratio of cycling female rats is at its lowest level during proestrus and highest during late estrus(1). This is in direct contrast to the present findings in the mouse. It appears that the increased T/S ratios in cycling animals may be due to a rise in blood levels of estrogen, since the exogenous administration of this hormone has been reported to increase I^{131} uptake(5,6) and T/S ratios (unpublished data). Also, Moon and Tur-

ner(7) have shown a reduction in thyroid function following ovariectomy and that estradiol prevents the decrease in thyroid secretion rate. Ovulation in both species is different in regard to its occurrence in the estrous cycle. In Wistar rats it occurs some 9-12 hours after onset of estrus(8). However, in albino mice it usually occurs about 2 hours after onset of estrus and sometimes earlier(9). Consequently, estrogen secretion probably occurs sooner and reaches a maximum concentration earlier in the mouse than in the rat. Therefore, the difference between the 2 species may be due to: 1) the release and/or increased concentration of estrogen occurring sooner in mice; or 2) a difference in thyroidal, or hypophyseal, or hypothalamic sensitivity to blood levels of estrogen.

The measurement of thyroid:serum iodide gradient is a very sensitive index of the level of circulating thyrotropic hormone(4,10). Therefore, it appears from our data that the maximum amount of TSH occurs during proestrus and the least amount during the first half of diestrus. However, in hypophysectomized rats injected with a single dose of TSH, the T/S does not increase for at least 6 hours. The maximal effect on the iodide pump occurs 1-2 days after injection of TSH (10,4). Hence the change in thyroid function during any one of the stages of the estrous cycle may in fact have been initiated during an earlier stage, since a transitory depression of T/S preceding its rise has been found to occur after injection of TSH into hypophysectomized rats(11). Another possibility is that TSH affects T/S at least in part through alterations of the organic iodine concentration in the thyroid(12). However, it is not known whether a substantial depletion of organic thyroidal iodine occurs during estrus, and if so whether such a change affects the T/S promptly.

Summary. The thyroid:serum radioiodide concentration ratio (T/S) was investigated in mice during the different stages of the estrous cycle. T/S was found to be at its lowest levels during diestrus and highest during proestrus. T/S values during the other stages of the cycle were intermediate and not significantly different from each other. The results indicate that the ability of the thyroid to concentrate iodide from the serum shows cyclic changes which can be correlated with stages of the estrous cycle. Also, the period of maximal thyroid activity is different from that previously noted in rats.

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