Thyroid and Adrenal Response to Varying Dose Levels of Epinephrine. (19385)

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It has become apparent that the release of the adrenocorticotropic and thyrotropic hormones for the anterior pituitary is dependent upon the physiological state and needs of the animal. The nature of the stimulus to the pituitary is still in question. The role of epinephrine in the release of these hormones has been considered by a number of workers (1-5). In the absence of quantitative data on the influence of epinephrine on the functional activity of the adrenal and thyroid, the present study was undertaken to determine and compare the simultaneous responses of these endocrine organs to varying dose levels of epinephrine.

Methods. Male rats of the Sprague-Dawley strain weighing 200-250 g were used. They were maintained on Purina laboratory chow and tap water until 18-24 hours before sacrifice, at which time they were deprived of food but allowed water *ad lib.* Two hours before sacrifice, each experimental animal was injected with 1.0 ml of epinephrine in 0.9% NaCl (containing 10, 20, 30, 50, or 100 μg of epinephrine.*), and each control was injected with 1.0 ml of saline. *Thyroid* I^{131} *Studies.* Four hours before sacrifice each rat was injected intraperitoneally with 1.0 ml of I^{131} solution containing approximately 5 microcuries of carrier free I^{131}† made to volume in phosphate buffer of pH 7.4. The animals were sacrificed by a sharp blow at the base of the skull and exsanguinated via a thoracic incision. The thyroid glands were removed, weighed and analyzed for their total and organic bound I^{131} contents according to the procedure of Botkin and Jensen(5). Control groups of 6 rats (saline injection) were run with each set of experimental animals (epinephrine injection). Groups of 12 or 24 experimental animals were used for each epinephrine dosage level. All values for I^{131} content were calculated as percent of the injected dose; those for the experimental animals are expressed as percentage deviation from control values and are illustrated in Table I.

TABLE I. Adrenal Cholesterol Content and Thyroid I^{131} Content After Epinephrine Injection. % deviation from control.

	μg epinephrine				
	10	20	30	50	100
Adrenal cholesterol	−6.2	−16	−19.9	−23.4	−30
Thyroid I^{131}	−5.7	−10.1	−15	−16.5	−24.1

Adrenal Cholesterol Studies. The animals were sacrificed by decapitation. Adrenals were removed, weighed and analyzed for total cholesterol by a modification of the method of Schoenheimer and Sperry(6). Control animals were run with each set of experimentals. Groups of 12 or 19 experimental animals plus 3 control animals were used for each epinephrine dosage level. All values were calculated as mg cholesterol per 100 mg adrenal wet weight; those for the experimental animals are expressed as percentage deviation from control values and are shown in Table I.

Results. Thyroid I^{131} *Studies.* Of the epinephrine dosages employed 10 μg produced a slight but not significant decrease in thyroid I^{131} content. With larger dosages there was an approximately linear decrease of I^{131} content of the gland from 10.1% below control values at 20 μg to 24.1% below control values at 100 μg (Table I).

Adrenal Cholesterol Studies. The decrease in adrenal cholesterol content observed after various levels of epinephrine injection paralleled very closely the degree of decrease found for thyroid I^{131} content. An insignificant decrease was produced by 10 μg. Progressively larger responses from 16.0% decrease at 20 μg

* Epinephrine Injection, U.S.P., 1:1000, Abbott Laboratories.

† The radioactive iodine(I^{131}) used in this investigation was supplied by the Oak Ridge National Laboratories on allocation from the Isotopes Division, U. S. Atomic Energy Commission.

to 30.0% decrease at 100 μg were found (Table I).

Discussion. The parallel responses of both thyroid I^{131} content and adrenal cholesterol content at the same short (2 hour) interval after administration of varying amounts of epinephrine might indicate a simultaneous stimulation of these endocrine organs. The question of whether the content of a hormone or its precursor in an endocrine organ is an accurate index of the amount of hormone released into the circulation must be considered in this connection.

The nature of the "epinephrine" stimuli which provoke an increased rate of release of adrenocorticotropin from the anterior pituitary has been actively investigated. Sayers(7) has expressed the view that this tropic hormone output from the anterior pituitary is regulated by the level of circulating target organ hormone. The metabolic effect of epinephrine may act to increase tissue utilization of the target organ hormones with a consequent lowering of venous titer of the hormones. Long and his associates(8,9) propose a biphasic mechanism whereby, in addition to regulation by the level of circulating target organ hormone, there is a direct stimulation of the pituitary by epinephrine.

It is possible that a mechanism of the type discussed above may also regulate the release of thyrotropic hormone from the anterior pituitary.

The apparent resulting increased release of both adrenocorticotropin and thyrotropin from the pituitary as suggested by the results of the present investigation probably cannot be maintained under all circumstances for an extended length of time but may give way to an increase of one at the expense of the other.

Summary. The smallest intraperitoneal dose of epinephrine which produces a significant response from the thyroid and adrenal glands of the rat in two hours (as measured by I^{131} concentration and cholesterol content respectively) is 20 μg. The responses observed with varying levels of epinephrine are quantitatively similar for the two glands and are approximately parallel between doses of 20 and 100 μg of epinephrine. This is interpreted as an increased rate of function of both glands. Various explanations of these findings are discussed.

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Serum Histaminase During Rabbit Anaphylaxis.* (19386)

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Rose and Weil(1) showed that anaphylaxis in the rabbit was accompanied by a sudden and marked decrease of blood histamine, and this was subsequently confirmed(6). Additional studies(2) showed that the decrease in histamine was confined not only to the blood, but occurred in tissues such as lung, liver and spleen as well. Because of the striking dis-

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