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THYROID AND ADRENAL RESPONSE TO VARYING DOSE
LEVELS OF EPINEPHRINE

*Subtask under Environmental Physiology, AMRL Project No. 6-64-12-028,
Subtask, Enzyme, Endocrine and Metabolism Studies in Shock.



MEDICAL RESEARCH AND DEVELOPMENT BOARD
OFFICE OF THE SURGEON GENERAL
DEPARTMENT OF THE ARMY

REPORT NO. 69

THYROID AND ADRENAL RESPONSE TO VARYING DOSE
LEVELS OF EPINEPHRINE*

by

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from

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Fort Knox, Kentucky

3 December 1951

* Subtask under Environmental Physiology, AMRL Project No. 6-64-12-028,
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ABSTRACT

THYROID AND ADRENAL RESPONSE TO VARYING DOSE LEVELS OF EPINEPHRINE

OBJECT

To determine and compare the simultaneous responses of thyroid and adrenal glands to varying dosage levels of epinephrine in relation to the release of pituitary tropic hormones under stress conditions.

RESULTS AND CONCLUSIONS

The smallest intraperitoneal dose of epinephrine which produces a definite 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 micrograms. 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 micrograms of epinephrine. This is interpreted as increased rate of function of both glands.

RECOMMENDATIONS

Investigation of the effect of epinephrine on function of thyroid and adrenal cortex should be studied by use of an in vitro technique employing studies of isolated glands incubated in nutrient media to clarify the mechanisms involved.

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THYROID AND ADRENAL RESPONSE TO VARYING DOSE LEVELS OF EPINEPHRINE

I. INTRODUCTION

It has become apparent that the release of the adrenocorticotrophic and thyrotropic hormones from 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, 2, 3, 4, 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.

II. EXPERIMENTAL

A. Methods

Male rats of the Sprague-Dawley strain weighing 200-250 grams 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.

1. Thyroid I¹³¹ Studies

Four hours before sacrifice each rat was injected intraperitoneally with 1.0 ml of I¹³¹ solution containing approximately 5 microcuries of carrier free I¹³¹* made to volume in phosphate buffer of pH 7.4. 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 micrograms of epinephrine**), and each control was injected with 1.0 ml of saline.

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 I¹³¹ 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.

*The radioactive iodine (I¹³¹) used in this investigation was supplied by the Oak Ridge National Laboratories on allocation from the Isotopes Division, U.S. Atomic Energy Commission.

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

All values for I^{131} content were calculated as percent of the injected dose; those for the experimental animals are expressed as the percentage deviation from control values and are illustrated in Table 1.

2. Adrenal Cholesterol Studies

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 micrograms of epinephrine) and each control was injected with 1.0 ml of saline. 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 milligrams cholesterol per 100 milligrams adrenal wet weight; those for the experimental animals are expressed as percentage deviation from control values and are shown in Table 1.

TABLE 1.

ADRENAL CHOLESTEROL CONTENT AND THYROID I^{131} CONTENT AFTER EPINEPHRINE INJECTION

Microgram Epinephrine	10	20	30	50	100	
Percent Deviation from Control	Thyroid I ¹³¹	-5.7	-10.1	-15.0	-16.5	-24.1
	Adrenal Cholesterol	-6.2	-16.0	-19.9	-23.4	-30.0

B. Results

1. Thyroid I^{131} Studies

Of the epinephrine dosages employed, 10 micrograms produced a slight (5.7%) but not significant decrease in

Thyroid I^{131} content. With larger dosages (20, 30, 50, and 100 micrograms) there was an approximately linear decrease of I^{131} content of the gland from 10.1% below control values at 20 micrograms to 24.1% below control values at 100 micrograms (Table 1).

2. 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 of 6.2% was produced by 10 micrograms. Progressively larger responses from 16.0% decrease at 20 micrograms to 30.0% decrease at 100 micrograms were found (Table 1).

III. 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 increased rates of release of adrenocorticotropin and thyrotropin from the anterior pituitary has been actively investigated. Sayers (7) has expressed the view that 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 target organ hormones with a consequent lowering of venous titer of the hormones. It has been suggested (8) that epinephrine acts to increase cortisone liberation, which then overrides the adrenaline response and results in a decreased uptake of I^{131} by the thyroid. Long and his associates (9, 10) propose a biphasic mechanism whereby, in addition to a direct stimulation of the pituitary by epinephrine, there is regulation by the level of circulating target organ hormone.

It is probable that the apparent resulting increased release of both adrenocorticotropin and thyrotropin from the pituitary as suggested by the results of the present investigation cannot be maintained under all circumstances for an extended length of time but will give way to an increase of one at the expense of the other. That this mechanism may depend upon the type of stimulus is shown by the response of a normal animal exposed to moderate cold for an extended period during which time the activity of both adrenal and thyroid are increased until the animal is adapted to his environmental.

IV. CONCLUSIONS

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 micrograms. 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 micrograms of epinephrine. This is interpreted as an increased rate of function of both glands. Various explanations of these findings are discussed.

V. RECOMMENDATIONS

Investigation of the effect of epinephrine on function of thyroid and adrenal cortex should be studied by use of an in vitro technique employing studies of isolated glands incubated in nutrient media to clarify the mechanisms involved.

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