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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appearance of naturally occurring histamine from these sites, it was decided to investigate the ability of this mechanism to deal with injected histamine. It was first noted that histamine injected either intravenously or by the intraperitoneal route produced an increase in the plasma histamine content which gradually disappeared over a period of minutes. If, however, the histamine was injected into previously sensitized rabbits, a marked and sudden disappearance of not only the preexisting but also of the injected histamine occurred following the injection of a shock dose of antigen(2). These findings made it clear that some powerful mechanism for the inactivation or "detoxification" of histamine was stimulated by the induction of anaphylaxis in this species. The present investigation was carried out in order to elucidate the nature of the mechanism involved.

Methods. Nineteen rabbits weighing between 2.5 and 3 kg each were sensitized to egg albumen. The egg albumen (Merck) was made up to a 3% solution in normal saline, and filtered before using. Each animal received 2 cc intraperitoneally every second day until five doses had been given. Two to three weeks after the last sensitizing dose, anaphylaxis was induced by the intravenous injection of 2 cc of antigen. The blood samples were taken by cardiac puncture both before and about 3-4 minutes after the injection of the shock dose when signs of anaphylaxis such as prostration, defecation and micturition were present. Each sample consisted of 20 cc, two of which were used immediately for histamine determination of the whole blood, and the remainder, after clotting, for histaminase analysis of the serum. The blood histamine was determined by the Code (3) modification of Barsoum and Gaddum's method(4), and is expressed as the base as γ/cc. The method of Ahlmark(5) was used for the histaminase determinations. Serum histaminase is expressed as γ histamine destroyed per cc plasma per hour. All determinations were done in duplicate.

Results. The results are given in Table I. The blood histamine values are in the left hand columns, and show the total blood histamine before and after the induction of shock. It will be seen that in all animals, with the exception of rabbit 19, a sharp decrease occurred. These results are confirmatory of those previously reported(1,2). In the right hand columns, the serum histaminase values are presented for the corresponding animals before and after the induction of anaphylaxis. Here it will be noted that a moderate to marked increase in activity of the serum histaminase was produced. Again, the one exception is in rabbit 19. The average control serum histaminase was 0.41 γ/cc/hr whereas following the induction of anaphylaxis the activity was 0.87 γ/cc/hr, which is an increase of 126%.

TABLE I. Rabbit Blood Histamine and Serum Histaminase Before and After Induction of Anaphylactic Shock in 19 Rabbits.

Blood histamine, γ/cc		Serum histaminase, γ/cc/hr		
Control	During shock	Control	During shock	% increase
—	.17	.55	.88	60
—	.22	.27	.75	178
—	.37	—	.98	—
—	.35	.37	1.25	238
2.1	.3	.37	1.12	200
—	—	.26	.84	222
1.73	.2	.26	1.06	308
3.6	.525	.39	.47	20
1.87	.17	.31	.83	68
1.5	.35	.43	.78	81
3.2	.25	.53	1.62	203
3.4	.55	.53	.66	24
3.8	.4	.49	.87	78
3.6	.4	.67	.81	21
3	—	.59	.80	35
2.88	.5	.49	1.34	174
4	.55	.29	.83	186
3.6	.4	.49	.78	59
4.6	4.4	.20	.18	0
	Avg	.41	.87	126

Signs of anaphylaxis were produced in the majority of animals, with death occurring in 12. There appeared to be no correlation between the intensity of the shock and the degree of change either in the blood histamine or serum histaminase values after induction of shock. The one exception was animal 19, in which there were no signs of shock, and little alteration of the blood histamine or serum histaminase values. It is also apparent that the reduction in blood histamine was more

consistent in degree than the corresponding increase in serum histaminase.

Discussion. These results support the view that the detoxification or inactivation of histamine which occurs following the induction of anaphylaxis in the rabbit may be due in part to an increase in the activity of the enzyme histaminase. It is likely that the source of this increased histaminase activity is from one of the parenchymal organs such as lung or kidney. Dragstedt and his co-workers(6) showed that when antigen was added to rabbit blood which was being perfused through isolated sensitized lung, there occurred a decrease in the blood histamine content. The histamine was probably being destroyed in the lung tissue although histaminase determinations of the tissue itself were not made. More recently, Carlsten *et al.*(7) have observed a high histaminase activity of lymph in dogs, the main source of which Carlsten(8) found to be kidney and gut. It is probable that another major factor contributing to the disappearance of blood histamine during rabbit anaphylaxis is the equally rapid disappearance of the white cell elements which takes place at the same time(2), since the bulk of blood histamine is contained in these cells in an inactive form (9). As discussed elsewhere(10), the production of anaphylaxis in the rabbit must be due to a release of histamine from cells into the plasma and not simply to the disappearance of histamine which occurs, for no symptoms occur when glycogen is injected intravenously into the rabbit although a rapid disappearance of blood histamine occurs(11). This is supported by the finding that addition of glycogen to rabbit blood *in vitro* does not alter the distribution of histamine, whereas the addition of antigen to sensitized rabbit blood *in vitro* causes a shift of histamine from the cells into the plasma(11).

Summary. 1. Studies on the blood histamine and the serum histaminase were made in a series of 19 rabbits before and after the induction of anaphylactic shock. 2. In all but one, a reduction of the blood histamine was produced following anaphylaxis. This confirms previous observations. 3. An increase in the serum histaminase activity was noted in all animals except the one in which there was no reduction of the blood histamine. 4. These findings support the view that the rapid disappearance of blood histamine which occurs during anaphylaxis in this species may be due in part to an activation of histaminase.

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