ported a similar result with normal serum inhibitor.

Experiments to clarify the origin of the progressive decrease in slope induced by virus (Fig. 1) have shown that (a) the slope effect is not attributable to the concentration of impurities (cf. 2) or to the accumulation of non-inhibitory reaction products; and (b) the inhibitor characterized by shallow slope does not sediment appreciably in centrifugal fields sufficient for sedimenting virus.

Discussion. The slope of the inhibition curves (Fig. 1) in the region of transition from zero to maximal agglutination may be tentatively interpreted in terms of the firmness of attachment of inhibitor to the particles of the *titrating* virus. Accordingly, virus-treated inhibitor may be described as a "weak" inhibitor in comparison with untreated inhibitor.

Available evidence suggests that the weak inhibitor is a free inhibitor, unattached to virus. Such an inhibitor could pre-exist in a heterogeneous inhibitor population and could be made manifest through a preferential action of virus against strong inhibitor. An attractive alternative is that the weak inhibitor is the product of a progressive, rather than all-or-none, action of virus. If the latter explanation should be correct, the demonstration of a free, weak inhibitor, intermediate between fully active and inactive inhibitor, would provide strong support for the enzymatic hypothesis of inhibitor inactivation by virus. The possibility that the action of virus is not all-or-none has been previously suggested by Burnet and collaborators[4,5] from related, but somewhat more complicated, experiments.

Summary. During the interaction of swine influenza virus and egg-white inhibitor of hemagglutination, there appears a weak inhibitor, which has titrating properties different from those of untreated inhibitor. This result renders impossible a simple kinetic treatment of the data. The significance of the weak inhibitor for the mechanism of virus-inhibitor interaction is discussed.

[4] Burnet, F. M., *Austr. J. Exp. Biol. and Med. Sci.*, 1948, **26**, 389.

[5] Anderson, S. G., Burnet, F. M., Fazekas de St. Groth, S., McCrea, J. F., and Stone, J. D., *Austr. J. Exp. Biol. and Med. Sci.*, 1948, **26**, 403.

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17102. Role of Adrenal in Uptake of I^{131} by the Thyroid Following Parenteral Administration of Epinephrine.

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In a previous paper[1] we reported that the parenteral injection of epinephrine into both the intact and the totally thyroidectomized dog resulted in an increase in secretion of thyrotropin from the adenohypophysis. In the intact dog this was evidenced by the development of hyperplastic changes in the thyroid following the daily injection of adrenalin-in-oil. Serum obtained from similarly treated totally thyroidectomized animals, when injected subcutaneously into young guinea pigs not exceeding 200 g in weight, resulted in hyperplastic changes in the thyroids of the treated guinea pigs.

It was further reported that the increase in circulating thyrotropic factor resulting from the injection of epinephrine in totally thyroidectomized dogs reached its peak approximately 4 to 6 days following the beginning of treatment, and thereafter began to diminish despite the continued injection of epinephrine.

The present report is concerned with a study of the role of the adrenals in the above described phenomena. In place of the biological assay method previously employed for the determination of circulating thyrotropin, we used the percentage uptake of parentally administered I^{131} as an index of thyroid activity. This technique has the relative ad-

[1] Soffer, L. J., Volterra, M., Gabrilove, J. L., Pollack, A., and Jacobs, M., PROC. SOC. EXP. BIOL. AND MED., 1947, **64**, 446.

vantages of simplicity and a higher degree of accuracy over the biological assay method.

Methods. Male rats of the Wistar strain (Carworth Farms) weighing approximately 125 g were employed. They were placed on a low iodine, minimally goitrogenic (Steenboch) diet* for at least 3 weeks before being used experimentally in order to insure an adequate uptake by the thyroid gland of I^{131}.[2] In the adrenalectomy experiments, rats of the Sprague-Dawley strain were also employed because of the reported lesser frequency of accessory adrenal tissue.

The experiments were planned to study the 24-hour percentage uptake of parenterally administered I^{131} by the thyroid gland after the administration of epinephrine in the intact and in the adrenalectomized animals. Some preliminary studies were conducted to determine the influence of the daily injection of 17-hydroxy-11 dehydrocorticosterone† upon the response of the bilaterally adrenalectomized animals.

All experiments were conducted with litter mates acting as controls. The animals in each experimental group were subjected to the same diet and environment and for the same duration of time, although the period of time that the respective groups were kept on the low iodine diet varied from experiment to experiment. In no instance, however, was such a period less than 3 weeks.

In the intact animals epinephrine was administered twice a day at 9:00 A.M. and 5:00 P.M., for 3, 7, and 32 days. Each dose consisted of 0.1 cc of 1:1000 aqueous epinephrine and 0.1 cc of epinephrine-in-oil, 1:500, injected subcutaneously in separate sites. The morning following the last injection of epinephrine (approximately 17 hours later) 2 microcuries of I^{131} was administered intraperitoneally. Twenty-four hours following the administration of the radioactive iodine the animals were killed by the intraperitoneal administration of Nembutal, and the thyroid glands removed.

In the experiments involving the adrenalectomized animals, the rats were bilaterally adrenalectomized after being on the low iodine diet for a period of not less than 3 weeks. At least one week was permitted to elapse following adrenalectomy before the injections of epinephrine were started. The adrenalectomized animals were maintained during the experimental period by the addition of sodium chloride to the drinking water, in isotonic concentration. Epinephrine was administered twice a day for 3 days in the same dosage given to the intact animals. In one experiment, one group of adrenalectomized animals received simultaneous injections of both epinephrine and 17-hydroxy-11 dehydrocorticosterone. The latter was administered subcutaneously in a dosage of 2 mg daily for 3 days.

The radioactive iodine was administered and the animals sacrificed in the same manner described for the intact animals. The thyroid glands were carefully dissected free of connective tissue weighed on a torsion balance, and placed in 2 cc of 1% sodium hydroxide. Digestion was carried out over a steam bath. The solution was diluted to 4 cc, an aliquot removed, placed in a metal cap, and allowed to dry. The β radiation of the sample was measured with a Geiger counter employing the original solution of I^{131} as a standard for calculation of the percentage uptake.

Results. In Table I are presented the results obtained in the intact animals. It will be noted that in each experimental group the percentage uptake of I^{131} is considerably greater in the control group than in the comparable group treated with epinephrine. The percentage uptake of I^{131} of the treated group varied from 45.3 to 66.8% of that of the untreated controls.

The injection of epinephrine (Table II) into the adrenalectomized animals, however, resulted in an increase in the percentage uptake of I^{131} as compared to that of the

* The Steenboch diet is as follows:

Yellow corn	76%
Wheat gluten	20%
Calcium carbonate	3%
Sodium chloride	1%
Irradiated yeast	4 g/k
Drinking water containing 0.06 μg KI/cc	

[2] Rawson, R. W., Tannheimer, J. F., and Peacock, W., *Endocrinol.*, 1944, **34**, 245.

† The 17-hydroxy-11-dehydrocorticosterone was kindly supplied by the Merck Co., Rahway, N. J.

TABLE I. Normal Rats.

Treatment with epinephrine, days	Epinephrine injected				Controls				% uptake of treated animals as compared to controls %
	No. of rats	Avg body wt, g	Avg thyroid wt, mg	Avg I^{131} uptake, %	No. of rats	Avg body wt, g	Avg thyroid wt, mg	Avg I^{131} uptake, %	
3	5*	140	9.2 ± 0.9§	7.3 ± 1.4	6*	149	10.1 ± 1.0	16.1 ± 5.5	45.3
7	6*	162	9.8 ± 1.5	12.4 ± 5.9	5*	187	11.2 ± 1.3	26.7 ± 4.3	48.3
32	6*	147	9.9 ± 2.3	23.7 ± 6.7	6*	162	11.3 ± 1.4	35.5 ± 6.3	66.8

TABLE II.
Adrenalectomized Rats.

3	4*	136	9.5 ± 0.4	23.6 ± 1.8	4*	139	10.4 ± 0.6	16.7 ± 6.4	141
3	3†	153	8.4 ± 1.0	27.6 ± 9.8	4†	157	9.6 ± 1.8	17.7 ± 2.8	156
3	3†	163	14.3 ± 0.7	28.0 ± 6.6	4†	170	12.0 ± 2.0	22.0 ± 4.8	127
17-hydroxy-11-dehydro-corticosterone	3†‡	163	14.1 ± 1.4	17.8 ± 1.0					81

* Wistar strain rats. † Sprague-Dawley rats. ‡ 2 mg daily for 3 days. §S.D.

non-injected adrenalectomized controls. In these experiments the percentage uptake of the administered I^{131} in the epinephrine treated adrenalectomized rats varied from 127 to 156% of that of the untreated adrenalectomized rats. In one small group of adrenalectomized animals injected with both epinephrine and 17-hydroxy-11-dehydrocorticosterone, there occurred a reversal of this phenomenon with a marked reduction in the uptake of radioactive iodine.

Conclusions. The injection of epinephrine into the intact rat results in a considerable decrease in the uptake of I^{131}. This is in sharp contrast to the results obtained in similarly treated adrenalectomized rats. In this group, the injections of epinephrine after adrenalectomy is followed by a pronounced increase in the percentage uptake of radioactive iodine. These experiments would indicate that the adrenal cortex exercises an inhibitory effect on the thyrotropin stimulating action of epinephrine. The results obtained in the rat are somewhat different from those observed in the dog, in that in the latter animal the inhibitory effects of the adrenal are not manifest until after several days of treatment with epinephrine. This apparently represents a species difference, although a different technique was employed.

In one preliminary group of experiments it was found that the parenteral administration of 17-hydroxy-11-dehydrocorticosterone, one of the carbohydrate acting fractions of the adrenal cortex, inhibited the thyrotropin stimulating effect of epinephrine.

That the decrease in uptake of I^{131} in the epinephrine treated intact animals is not due to the vasoconstrictor effects of the epinephrine is evidenced by the fact that in similarly treated adrenalectomized animals the percentage uptake of I^{131} is considerably greater than that of the untreated controls. A period of 17 hours after the last injection of epinephrine was allowed to elapse before the administration of I^{131} in order to avoid any possible vasoconstrictor effects.

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