THE PART PLAYED BY ADRENALIN IN THE REFLEX CONTROL OF THE THYROID GLAND

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In previous investigations [2, 3] we demonstrated the relationship between the condition of the central nervous system and the secretory cycle of the thyroid. It was found that during emotional excitement secretion of hormonal iodine from the thyroid was stimulated and its absorption inhibited.

We presumed that these changes were brought about by the liberation of large amounts of adrenalin into the bloodstream. This view was based on the results of Cannon and De la Paz [7] which showed that excitement causes liberation of adrenalin into the blood.

To confirm our hypothesis, we have investigated the effects of intramuscular and intravenous injections of adrenalin on the thyroid secretory cycle.

Several descriptions have been given of the effect of adrenalin on the absorption of radioiodine by the thyroid [5, 6, 8, 9]. This work has shown that adrenalin inhibits the accumulation of radioiodine in the gland. In the investigations referred to, no attention was paid to the effect of adrenalin on thyroid secretory function. We have found no references to any such investigations having been made.

The thyroid secretory cycle consists of two phases – one of hormone formation and the other of its secretion; the authors mentioned above used a method which allowed only one of the two phases to be studied. It is nevertheless evident that any study in which the functional condition of the thyroid is inferred purely from observations made on the uptake of radioiodine necessarily is inadequate.

METHOD

The experiments were carried out on 8 dogs. Intramuscular or intravenous injections of 0.15 mg/kg 1:1000 adrenalin were given. In most of the animals this amount of adrenalin caused a dilatation of the pupils, breathlessness, spasm of the peripheral vessels, vomiting movements, and sometimes actual vomiting. This reaction usually lasted up to 5 minutes, after which the animal settled down again. Since there is considerable variability in the sensitivity to adrenalin, in some cases in order to obtain the reaction described it was necessary to increase the dose of adrenalin up to 0.16-0.17 mg/kg weight.

Radioiodine was given orally, the amount usually being 0.7-0.8 μC/kg weight.

We studied thyroid secretion before injecting adrenalin, and counted the number of impulses over the thyroid gland; the figure obtained was taken as representing the initial radioactivity. After the adrenalin injection, we measured the radioactivity after 15 and after 30 minutes, and then hourly for 3-4 hours, i.e., until it had returned to its original level. Here it must be realized that variations in thyroid radioactivity up to ± 10% were also found under physiological conditions; no attention was paid to any variations of this order occurring in the experiments.

RESULTS

In the first set of experiments we studied the utilization of radioiodine by the thyroid under normal conditions and after an adrenalin injection. Normally, the rate of uptake of radioiodine by the thyroid shows considerable variation, and we therefore decided to study its absorption in the same animal before and after the adrenalin injection. On each ocasion, the animal was used for an experiment only after the whole of the previously injected radioiodine had been eliminated from the thyroid.

It can be seen from the results given in the table that normally after an injection of radioiodine, the amount of it in the thyroid gradually increases; after 4 hours, as a rule the radioactivity of the gland has reached almost twice the values shown during the first hour. The amount absorbed 24 hours after the injection (maximal absorption) was between 21.8 and 35.4% of the total amount injected. These values lie within the normal physiological limits.

After the adrenalin injection, the utilization of radioiodine by the thyroid gradually fell. The effect

Effect of Adrenalin on the Radioactivity of the Thyroid Gland (Figures give the percentage absorption of the total radioiodine injected)

Date of experiment	Before (A) and after (B) injecting adrenalin	Time, in hours					Name of dog
		1	2	3	4	24	
12/XI 1957	A	4,0	5,5	7,6	8,2	21,8	Jack
27/III 1958	B	4,6	5,7	5,6	5,6	13,1	
18/VII 1958	A	8,8	11,2	12,4	14,7	30,6	Coward
21/XI 1958	B	8,4	9,6	9,6	10,0	20,7	
19/IX 1958[1]	A	10,5	12,4	14,2	15,2	35,4	Beetle
1/XII 1958[1]	B	2,6	4,3	5,3	6,3	10,0	
14/I 1958	A	3,0	4,2	5,3	6,5	25,5	Blondy
26/III 1958	B	5,9	6,6	6,9	7,1	15,1	
4/IV 1958	A	3,8	8,8	9,9		22,2	Bobtail
23/V 1958	B	3,9	5,8	7,4	8,2	19,2	

[1] Adrenalin injected intravenously.

was usually apparent during the second hour of uptake. The low level of utilization was found not only during the first few hours of uptake, but even after 24 hours. Thus the maximal absorption was considerably less than normal.

This phenomenon was particularly well shown after the simultaneous intravenous injection of radioiodine and adrenalin (see table, experiment 1/XII/1958).

When it is realized that adrenalin is readily oxidized, such a prolonged action at first sight appears unexpected. However it can readily be explained as follows: According to A. M. Utevskii [4], the physiological action of adrenalin does not terminate with its breakdown, and evidently in this case we are concerned not with the action of adrenalin itself but with that of its breakdown products.

Haigh, Reiss, and Reiss [8] have demonstrated a similar effect of adrenalin on the utilization of radioiodine by the thyroid. They found that if adrenalin is injected 30 minutes after giving an iodine injection there is a fall in the absorption curve. This result indicates a reduction in the utilization of radioiodine by the thyroid.

The amount of iodine taken up by the gland is an index of the rate of hormone formation; therefore the studies described lead us to suppose that under the influence of adrenalin the hormonal function of the thyroid is depressed.

However it is still not clear as to whether the values found for the maximal absorption (under the influence of adrenalin) represent a reduction in the rate of hormone formation or whether the effect is due to a more rapid secretion of the hormone from the gland. To answer this question it became necessary to obtain results on the secretory function of the thyroid under the same conditions. The second set of experiments was designed to determine the effect of adrenalin on hormonal liberation.

Once more adrenalin was injected intramuscularly and intravenously. The same result was obtained in each case, and we therefore report only the results for the intravenous injections. It can be seen from Fig. 1 that the action of adrenalin on the hormonal liberation occurs after only 15 minutes and the action is maintained for 1-2 hours. After this time, as a rule, the radioactivity of the gland returns to its initial level.

Only in 17 out of the 55 experiments did we find any noticeable change in secretory function. In the remaining experiments the action of adrenalin was very marked, and in some, the reduction in radioactivity amounted almost to 40% of the original value.

In order to determine the effects of the injection as such and the experimental conditions themselves on the thyroid function, we carried out a series of control experiments in which physiological saline was injected. It was found that the latter had no effect on thyroid function. The change in radioiodine content was not greater than ± 10%.

In assessing the results of the second experiment, it can be seen that adrenalin stimulates liberation of the hormone from the gland into the bloodstream. This in turn shows that the reduced utilization of radioiodine by the thyroid 24 hours after the adrenalin injection is a result not only of the suppression of hormone formation but also of the increased amount liberated.

We also thought it important to find in what way the action of adrenalin in stimulating hormone secretion is brought about. Is the effect, as some people consider, mediated by the hypophysis, or does adrenalin exert an influence on the thyroid directly ?

A. L. Botkin and H. Jensen [5] showed that after adrenalin has been injected both the iodine in the blood plasma and that bound to protein is considerably reduced. They consider that adrenalin brings the body into a condition in which the utilization of thyroid hormone by the tissues is increased, and this in turn leads to a loss of hormones from the blood. This loss has the further effect of increasing the secretion of thyrotropic hormone by the hypophysis, which causes

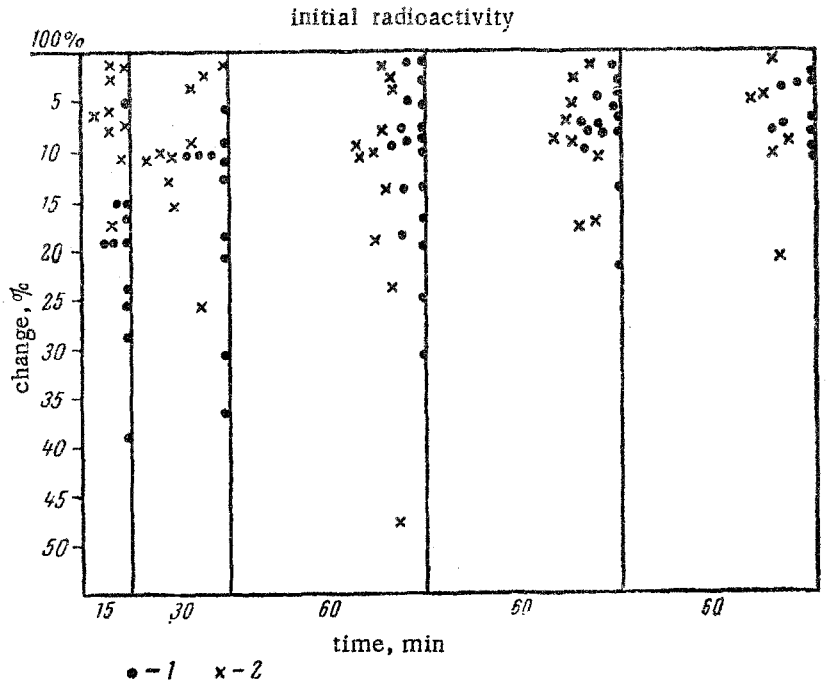

Fig. 1. Effect of adrenalin on the liberation of hormonal iodine from the thyroid (before and after removing the anterior hypophysial lobe). 1) Intact dog; 2) after removal of anterior pituitary lobe.

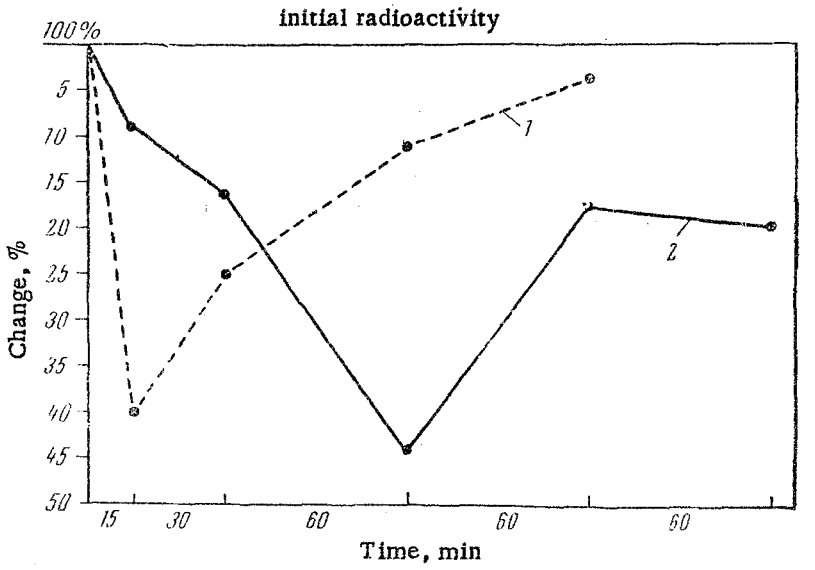

Fig. 2. Effect of adrenalin on the radioiodine content of the thyroid in (1) normal and (2) hypophysectomized dogs.

an increased liberation of thyroid hormone. If this interpretation is true, then it is clear that after removal of the anterior pituitary lobe there ought to be no increase in thyroid secretion.

The experiments carried out on animals after removal of the anterior lobe of the pituitary showed that the injection of adrenalin just as in the case of unoperated animals causes an increased secretion of thyroid (see Fig. 1).

A marked feature of the operated animals was that the radioactivity of the gland after the intravenous adrenalin injection fell not after 15 minutes, but after 40 minutes or even later. Figure 2 shows the results of one of these experiments. The delay in the reaction is understandable when it is realized that hypophysectomy causes a marked reduction in the functional activity of the thyroid.

The response of the thyroid gland to adrenalin after removal of the hypophysis shows that if adrenalin acts on the thyroid as described by A. L. Botkin and H. Jensen, then it must act in some other way also. It therefore seems logical to admit the existence of another mechanism. It is possible that adrenalin acts indirectly on the thyroid. B. V. Aleshin [1] showed

the effect of adrenalin on thyroid tissue in vitro. By incubating pieces of thyroid in a Warburg apparatus to which adrenalin had been added, they observed that the adrenalin had a stimulating effect.

Our experiments have shown that adrenalin changes the functional condition of the thyroid. These changes are similar to those which we found previously to occur during emotional excitement. This fact gives reason to suppose that during excitation adrenalin entering the bloodstream may be one of the mediators of the influence exerted by the central nervous system on the thyroid gland.

Under normal physiological conditions increase in hormone formation and increase in the rate of liberation take place together; similarly, when hormone formation is slowed down, there is also a reduction in the amount liberated. Under conditions when the adrenalin content of the body rises, besides inhibition of hormone formation by the thyroid there is also stimulation of the liberation of the hormone into the bloodstream. The results obtained are important because they enable us to envisage the possibility that the formation and the liberation of the hormone may be influenced in opposite directions; also they confirm that adrenalin stimulates thyroid function.

Previous investigators [5, 6, 8, 9, 10] in studying thyroid function purely in terms of absorption, necessarily came to the opposite conclusion because, as our investigations have shown, adrenalin inhibits formation of the hormone. We have supposed that the reduction in the hormone formation which occurs together with an increase in its rate of liberation represents a "physiological measure," but that the true function of the thyroid under these conditions must be evaluated in terms of its liberation into the blood. It is known that the deciding factor in the activity of any gland including the thyroid is the amount of hormone passing into the bloodstream; it is in this way that the participation of the endocrine glands in the adaptive reaction of the body is determined and their role in the general process of regulation decided.

SUMMARY

A study was made of the part played by adrenalin in the transmission of central nervous influences through the thyroid gland.

Injections of adrenalin decreased the absorption of radioactive iodine by the thyroid and stimulated the liberation of the hormone from it. It had been shown previously that similar effects occur during emotional excitement.

From the effect of adrenalin on the secretory cycle of the thyroid it was concluded that adrenalin is one of the mediators of central nervous control of the thyroid.

Adrenalin may also act on the thyroid without participation of the hypophysis.

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