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Increased Resistance to Anoxia After Thyroidectomy and After Treatment with Thiourea.

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Several reports have shown that removal of the thyroid increases the resistance of the rat to anoxia, presumably because this operation reduces the consumption of oxygen.[1-5]. However, some authors were unable to find differences between normal and thyroidectomized rats exposed to low oxygen pressures.[6,7] Our first investigation of this problem was made on thyroidectomized rats which had been fasted overnight to reduce their oxygen consumption to a basal value; the resistance of these rats to anoxia did not significantly differ from that of intact controls similarly fasted. Meanwhile, it was found that fasting itself affects the sensitivity to low oxygen pressures.[8,9] It was therefore necessary to expose to anoxia fasted and fed thyroidectomized rats concomitantly with similar groups of intact animals. Similar tests were carried out in animals treated with thiourea, a drug preventing the thyroid from releasing its hormone.[10,11] Since it was also desired to examine the effect of metabolic stimulations on resistance to anoxia under controlled feeding conditions, parallel experiments were carried out in animals treated with thyroxine or dinitrophenol. Both the thyroid hormone[3,12,13] and dinitrophenol[3,14] were previously reported as decreasing the resistance to a low oxygen pressure.

For the anoxia tests, the animals were placed in a continuous-flow low pressure chamber (21-24° C), where they were kept for 15 minutes at each one of the following pressures in succession: 200, 175, 150, 125, and 100 mm of mercury.[8,9] The resistance to anoxia was estimated by measuring the length of survival in minutes counting from the beginning of the experiment. For instance, a survival of 12 minutes indicates that the animal died at the pressure of 200 mm; a survival of 56 minutes shows that death occurred after 11 minutes at the pressure of 125 mm (Fig. 1). The averages for the survival of each group are reported in the tables with their standard errors; these were helpful in interpreting the results, although their significance was somewhat affected by the fact that the variations of the stimulus (pressure levels) were not continuous.

Part of a group of male rats weighing from 50 to 80 g were thyroidectomized, the rest being kept as controls. The anoxia tests were performed one month later. All the animals were left without food overnight, and then separated into 4 groups of 6 animals each. One normal and one thyroidectomized group remained unfed, while another normal and another thyroidectomized group received food for one hour. All were exposed to the low oxygen pressures 3 to 4 hours after the feeding period. The results (Table I) show that

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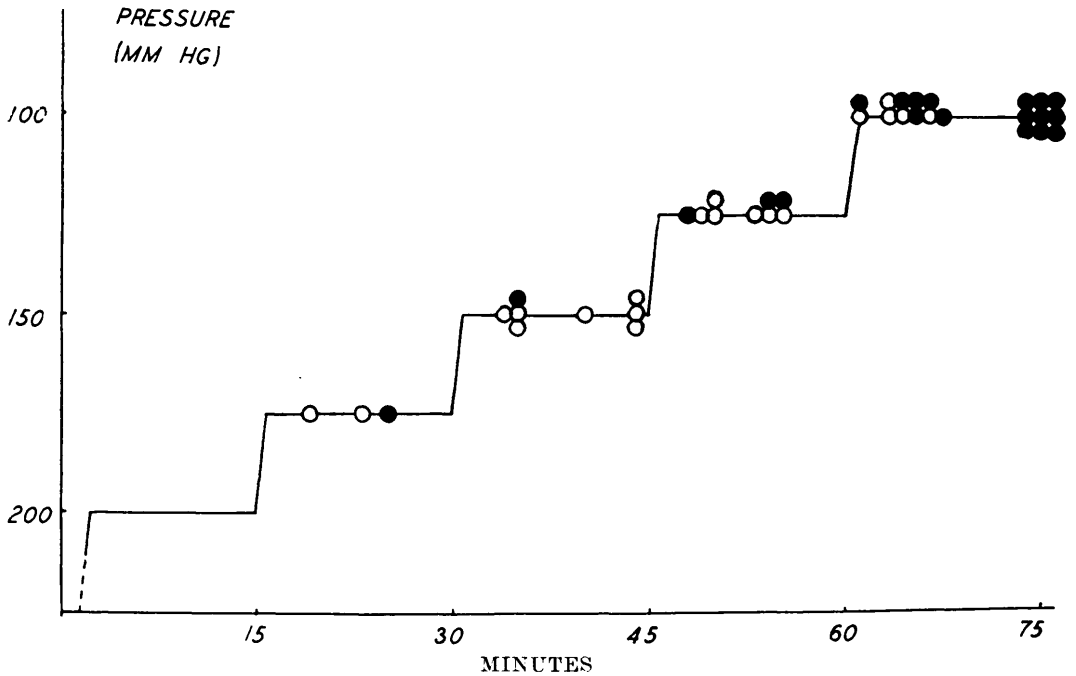

FIG. 1.
Survival of normal and thyroidectomized rats at various levels of reduced pressure. Each circle indicates the death of a rat; the light circles referring to the controls and the dark circles to the operated animals.

fasted animals, whether normal or thyroidectomized, were considerably less resistant to anoxia than fed animals, no differences between intact and operated animals being apparent in the fasted groups. However, the fed thyroidectomized rats withstood anoxia much better than the fed controls.

In all the following experiments (Table II), the animals were fasted overnight, fed during one hour, and exposed to the low pressures 3 to 4 hours later. The presence of a large amount of food in the stomach was ascertained at autopsy. The greater resistance to anoxia in thyroidectomized animals was confirmed, using a group of 20 rats operated from 6 to 8 weeks previous to the test (Table II, Fig. 1). Another group of rats received a 1% solution of thiourea in drinking water for 3 months; these proved much more resistant to anoxia than their controls (Table II). No controls but almost half the thyroidectomized and thiourea-treated rats survived to the end of the test. On the other hand, the resistance to oxygen deficiency was markedly decreased in rats treated either by 0.2 mg of thyroxine daily for 3 weeks or by a single injection of 25 mg of dinitrophenol per 100 g of body weight 30 minutes before exposure to the low oxygen pressures (Table II).

The opposite effects of thyroidectomy and thyroxine treatment on resistance to anoxia were probably mediated through metabolic variations, since dinitrophenol, a metabolic stimulator without effect on thyroid defi-

TABLE I.
Resistance of Fed and Fasted Thyroidectomized Rats to Anoxia.

Duration of fast (hr)	Operation	Avg body wt (g)	Avg survival (min) ± standard error
3	None	125	55.5 ± 3.5
22	"	121	28.3 ± 4.2
3	Thyroidectomy	83	69.2 ± 3.9
22	"	79	31.4 ± 5.3

TABLE II.
Effects of Various Metabolic Agents on Resistance of Rats to Anoxia.

	No. of animals	Avg body wt (g)	Avg survival (min) ± standard error
Controls	20	192	47.3 ± 3.4
Thyroidectomized	20	118	64.0 ± 3.2
Controls	7	279	50.4 ± 2.7
Thiourea	9	155	68.0 ± 3.2
Controls	6	267	44.3 ± 3.2
Thyroxine	6	225	26.5 ± 4.1
Controls	6	193	44.2 ± 3.7
Dinitrophenol	6	197	12.1 ± 4.8

ciency,[15,16] decreases the resistance to low oxygen pressures as does thyroxine. However, in the animals fasted for one day, the effect of metabolic variations on anoxia resistance was overshadowed by the increased sensitivity to anoxia resulting from the fast.[8,9]

Conclusions. (1) Thyroidectomy increases the resistance of the rat to anoxia; but only in fed animals. (2) Treatment with thyroxine decreases the resistance of the rat to anoxia. Since dinitrophenol, a metabolic stimulator without effect on thyroid deficiency, also decreases the resistance to a low oxygen pressure, the role of the thyroid in conditions of anoxia appears mediated through the effect of this gland on metabolism. (3) Animals given a 1% solution of thiourea in drinking water show a marked increase in resistance to anoxia probably as a consequence of the suppression of thyroid function due to this drug.

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Inhibition of Growth of Typhus Rickettsiae in the Yolk Sac by Penicillin.

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The results to be reported here were obtained in one of a series of experiments designed to test the effects of various enzyme inhibitors and activators on the intracellular multiplication of rickettsiæ. The yolk sac of the developing hen's egg (Cox[1]) was chosen as the medium for this work because of its uniformity and economy.

Material and Methods. A murine strain of typhus rickettsiæ, in its 8th and 9th passages in fertile eggs, was used. 36 eggs were injected, 18 of which were treated with penicillin, while 18 served as controls. All eggs were incubated at 37°C.

A yellow powder containing the sodium salt of penicillin was dissolved in distilled water. In the first experiment 0.2 cc of this solution, containing 325 Oxford units, was injected into the yolk sacs of 6 eggs on the 2nd, 4th, and 6th days after injection with rickettsiæ. In the second experiment, similar injections were given to 12 eggs on the 3rd, 5th, and 7th days after injection with rickettsiæ.

The eggs were studied for the presence of rickettsiæ at intervals after injection. When an egg in either the control or the treated series showed evidence of fetal death, it was opened for study, and usually an egg in the corresponding series was opened and studied simultaneously. In Experiment 1, when the

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