Significance of Thyroid in Cold Survival of Hamsters* (32814)

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Extirpation of the thyroid gland of rats lowers basal metabolism in a thermoneutral environment (1). However, this gland is not necessary for the increased metabolic rate which accompanies acute exposure to cold (2,3). Despite the increase in metabolic rate in thyroidectomized (ThX) rats, they cannot survive exposure at 5°C for more than 6–8 days (4,5).

In the hamster, Chaffee *et al.* (6) found that ThX hamsters survive prolonged cold (—12 to —18°C) for weeks at a time, and Yousef *et al.* (7) reported that hamsters after exposure for 1 week to 5°C maintained a higher metabolic rate. Also unlike the lowered liver mitochondrial P:O ratios reported in cold acclimated rats, which were associated with possible increase in thyroid function (8,9), there is some evidence that in the hamster there may be conversely a significant elevation of the P:O ratio (10). In addition, there is unquestionably a higher liver mitochondrial per cent acceptor effect (11). Thus, the evidence seems to indicate that increased metabolic rate may not be due to an enhanced thyroid activity in the hamster, and that increased thyroid activity in this animal may not be essential for cold survival.

The objective of the following study was to gain more information about thyroid function as a factor in the survival of hamsters exposed to a severe cold environment.

Materials and Methods. Two experiments, A and B, were conducted; each involved 10 control hamsters (Group I), 8 surgically thyroidectomized animals (Group II) and 8 animals thyroidectomized by radioactive iodine (^{131}I) (Group III). Surgical thyroidectomy was performed under ether anesthesia. The hamsters were thyroidectomized in Exp. A at the age of 8 weeks and in Exp. B at the age of 4 weeks. Thyroidectomy by radiation was performed by injecting each animal intraperitoneally with 1000 μC ^{131}I. The controls were sham operated leaving the thyroid intact. Until complete recovery all animals were kept at room temperature and had free access to food, Rockland complete rat diet in pellet form, and water. In Exp. A the animals were exposed to a cold temperature of —6 ± 1°C for a period of 3 weeks. In the second Exp. B the animals were bled by heart puncture for protein-bound iodine (PBI) determinations 6 days prior to 3 weeks exposure to —8 ± 2°C. The animals were supplied with apples and lettuce since in the cold room the water, though frequently changed, often froze.

Oxygen consumption of all animals was measured at —6°C in Exp. A as previously described (7) at exactly 6 hours after first being exposed to cold. In Experiment B protein-bound iodine (PBI) was determined in plasma of the animals using the dry ash method (12). Body weights were taken before and after exposure to cold. Survival time was determined as the time between the initial exposure and death of the animal.

Results and Discussion. In both Exps. A and B when the animals were exposed to —6°C, oxygen consumption increased significantly in all three groups (Table I). This indicates that the rapid increase in metabolic rate at this severe temperature can occur without an increase in the rate of thyroid secretion. This augmented metabolic rate may be due to greater muscular tonus, shivering, and increased adrenaline or nor-adrenaline secretion rate. The data on survival at cold temperatures (—6°C to —8°C) of both experiments are shown in Fig. 1. It is clear that the animals thyroidectomized by radiation (Group III) were not able to survive the

* Contribution from the Missouri Agr. Extpl. Sta. Journal Series No. Approved by the Director. Supported in part by the SSRC of the Univ. of Missouri; U.S. Army Contract No. DA-17-67-C0025; and USAF Aeromed. Res. Command, Contract F 29600-56-C-0009.

TABLE I. Plasma PBI, O_2 Consumption and Body Weight of the Control, Surgically-ThX, and Radio-ThX Hamsters.[a]

Animals	Oxygen consumption (ml/gm per hour)		PBI (μg/100 ml)	Body wt. (gm)	
	21°C	−6°C		21°C	−6° to −8°C[b]
Group I	1.21 ± .04	5.43 ± .07	3.9 ± .21	105.7 ± 2.2	82.9 ± 3.4
Group II	0.93 ± .03	4.23 ± .09	1.6 ± .26	94.7 ± 3.7	74.8 ± 4.2
Group III	1.00 ± .04	4.30 ± .11	0.8 ± .15	87.8 ± 3.2	72.1 ± 3.5

[a] Values ± SE.

[b] Animals were weighed at end of exposure to cold. Those that died were weighed within a few hours of death.

cold temperatures. More than 68% of this group died within the first 72 hours of exposure and all except one died within 6 days. None of the hamsters in Group I or Group II died during the first 9 days of exposure to cold. After 10 days and thereafter, more than 50% of Group II and 85% of Group I died. The death of these animals may be due to a failure of heat-producing mechanisms, thus decreasing their ability to maintain a high level of metabolic rate for a period longer than 10 days.

A comparison of the normal and surgically thyroidectomized animals seems to suggest that thyroid function is not significant for cold survival. Reported increases in TSR at cold temperatures could be due to higher excretion of thyroxine in the feces (13). Chaffee *et al.* (6) reported the survival of surgically ThX hamsters for as long as 6 weeks at −12°C, but this may have been due to the Purina Chow pellets, which have since been shown to contain thyroxine (13). However, poor survival of the ^{131}I thyroidectomized hamster suggests the existence of ectopic thyroid tissue in the hamster. Recently, Taurog and Evans (14) have reported that formation of thyroxine is entirely independent of specialized thyroid tissue and suggested the intestine as a possible site of thyroxine formation. These findings are reminiscent of the work of Morton *et al.* (15) which indicated that ThX animals are capable of producing thyroid hormones. Our data on the PBI of the 3 groups studied (Table I) indicated that Group II animals had a significantly lower PBI than Group I, and a higher PBI than Group III. This further indicates that the surgically ThX hamsters may produce the needed level of thyroxine to resist the cold stress. However, the radio-ThX animals presumably lost their ectopic thyroid tissue and did not have the needed level of thyroxine to maintain their cellular metabolic processes, resulting in failure to resist cold stress.

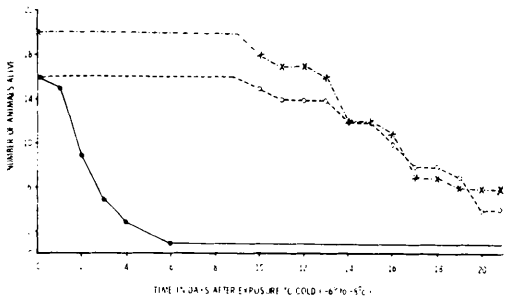

FIG. 1. Cold survival of radio-thyroidectomized (●), surgically (○), and sham-thyroidectomized (×) hamsters.

All 3 groups of animals lost body weight during exposure to cold. The higher loss of body weight in Group I and II (Table I) is possibly due to the longer period of survival in the cold environment.

Summary. All three groups of hamsters were exposed to a cold temperature of −6° to −8°C. Group I served as a control; Group II were thyroidectomized by surgery; and Group III were thyroidectomized by ^{131}I. Exposure to cold causes a significant increase in oxygen consumption and a decrease in body weight of all 3 groups. Animals in Group I and II survived for more than 9 days; however, 68% of the animals in Group III died

within 72 hours after exposure to cold. The plasma PBI in Group II was lower than in Group I and higher than in Group III. This suggests that the hamster likely has ectopic thyroid tissue which enhances survival of thyroidectomized animals. A comparison of control and surgically-ThX animals suggest that the known increases in TSR at cold temperatures are not significant in survival to extreme cold.

Further investigations should test the value of thyroxine replacement of survival of the radio-thyroidectomized animals and a comparison on propyl thiouracil and thyroxine-supplemented intact animals when exposed to extreme cold.

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Received July 14, 1967. P.S.E.B.M., 1968, Vol. 127.

Studies on Phosphorylase Activity in the Rat Ductus Deferens* (32815)

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In skeletal muscle, low levels of phosphorylase *a* activity are obtained when manipulative stimulation of the tissue is kept minimal prior to assay and when ethylenediaminetetraacetic acid (EDTA) is employed in the homogenizing medium which prevents the *in vitro* conversion of phosphorylase *b* → *a* by inhibiting phosphorylase *b* kinase (1). The extent to which these factors affect phosphorylase *a* activity in the smooth muscle of the rat ductus deferens has not been clearly established. Phosphorylase *a* activity determined shortly after removal of the ducts from rats was eight times greater than that found in ducts placed in a warm, aerated, saline bath for 30 min prior to assay (2). Treatment with EDTA had no effect on levels of phosphorylase *a* activity determined in these ducts (3). The results of further studies on the effects of manipulation and EDTA on phosphorylase *a* activity in the rat d. deferens will be presented.

Methods. Large adult intact rats and some castrated for 6 days were used. The procedure for removal of the ducts and trimming before freezing with solid CO_2 and the method of suspending them in Krebs–Ringer–bicarbonate–glucose medium, gassed with 95% O_2, 5% CO_2 were described previously (2). To remove, trim, and express the sperm from each duct requires 35–40 sec and these ducts are designated as "manipulated." Ducts removed and frozen with solid CO_2 immediately (within 3–5 sec) then trimmed in the frozen state before assay, are designated "quick-frozen." When ducts were to be stimulated electrically, they were suspended on hooks (2), the electrodes placed at the ends of the ducts and shocks given for 10 sec (30 V/

* Aided by a grant from the USPHS (AM-04965-06) Natl. Inst. of Arthritis and Metabolic Diseases and Muscular Dystrophy Assoc. of America, Inc.