synthesis as determined by ^{3}H-Thymidine incorporation. (The isotope was administered 2 h prior to sacrifice.) Removal of RNA did not decrease the ratio of experimental to control radioactivity.

In Figure 2 radioactive nuclei can be seen in the experimental (2a) but not in the control; radioactive mitotic figures were also seen more frequently in the former than in the latter.

Experiments pursued during the springtime (March-April) on populations of northern Canadian origin gave different results. These animals had almost no mitotic figures in their lenses when they first arrived at the laboratory but the mitotic index began to increase during the ensuing weeks. When the organisms were given T_3 only the lens, among the organs studied, displayed more hyperplastic activity. This result may be due to a temperature change witnessed by the animals in their native locale or in transit to the laboratory.

In a previous report, we suggested that the increase in temperature occuring during the spring might cause anterior pituitary outflow mediated by hypothalamic releasing factors[15]. The 'non-responsive' organisms may have already produced enough TSH to arouse considerable mitotic activity in most tissues so that additional T_3 could produce no further increase in the magnitude of the effect. This possibility will be tested in experiments upon hypophysectomized and thyroidectomized specimens but is, in any event, a prediction of the thermoendocrine hypothesis we presented elsewhere[15].

The question whether the amount of T_3 and T_4 administered is in the physiological as opposed to the pharmacological range has yet to be satisfactorily resolved. The frogs do, however, have enough endogenous T_3 and/or T_4 to produce the effects observed. Thus, when TSH (0.002 U/g) was injected, mitotic activity in the lens increased by a factor of three. So far we have not studied this response in other organs.

Despite much study the mechanism of action of T_3 and T_4 is unclear[16]. Initial data we have secured suggests that genomic activation may account for our findings. Within an hour after T_3 administration, the nuclei of lens epithelial cells exposed to ^{3}H-actinomycin D showed an increased level of binding of the antibiotic. It has been suggested that actinomycin D can be used as a probe for gene activation[17]. In earlier studies of injured and cultured frog lenses, we have shown that increased ^{3}H-actinomycin D binding takes place in advance of heightened syntheses of RNA[18-20]. Whether this will also prove to be the case in the T_3 stimulated system is at present unknown but the matter will be investigated shortly.

On the basis of the initial data it seems, the increase in the number of division figures takes place because more cells have entered upon active traverse of the generative cycle (i.e., the growth fraction has been amplified by the hormone). In the South Dakota frogs which do not possess any measurable mitotic index in the lens, this must be the case for almost all the cells (as determined by microspectrophotometry and autoradiography) exist in G_1. As we will show explicitly, in a later publication, introduction of T_3 shifts many cells through the S, G_2 and M states.

Zusammenfassung. Nachweis, dass bei adulten, reifen Fröschen Thyroxin und Triiodothyronin die mitotische Aktivität und die DNS-Synthese in verschiedenen Organen (Augenlinse, mit Epithel, Niere Darm, Leber, Milz, Haut, Horn- und Nickhaut) zu stimulieren vermag.

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A Comparative Study of the Calorigenic Action of Noradrenaline in the Rat and Ground Squirrel Adapted to Different Temperatures

The effect of noradrenaline was examined in rat, guinea-pig and mouse[1-4,5], but in hibernators this effect was not systematically studied. Some data on the seasonal changes concern the sensitivity of a hibernator to injected noradrenaline[6].

Materials and methods. Observations were made on 4 groups of adult albino male rats of Wistar strain and on 4 groups of ground squirrels weighing 200–260 g, each consisting of 8 to 10 animals. Rats were adapted to 4 °C, 30 °C or 36 °C and the ground squirrels to 30 °C or 36 °C for about 4 weeks. One group of ground squirrels was examined after being artificially aroused from hibernation in October. Noradrenaline (Galenika) was injected i.p. in doses of 1.6 mg/kg of body wt. Control groups were injected only with physiological solution. The oxygen consumption was measured individually in a gas analyser[7], 30 min before the injection of noradrenaline and after the injection over the period of the duration of the effect. All measurements were realised at 30 °C.

Results and discussion. Results are expressed in calories per m^2/24 h and summarized in Figures 1 and 2 together with the initial values obtained prior to the injection. In the rats adapted to 4 °C or to 30 °C, a significant increase in the heat production was observed 10 min after the injection of noradrenaline, being 46% and 30% respectively. Compared with the data of some other authors

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(JANSKY et al.[1], HOŠEK and NOVAK[3], HSIEH and CARLSON[8]) this high level of the heat production persisted longer in our experiments and reached a maximum in both cases about 60 min after the injection. For cold-adapted rats, this maximal increase was 68% and for those adapted to thermoneutral zone it was 54%. Body temperatures increased under the influence of noradrenaline in both groups, reaching 39 °C in the animals adapted to the thermal neutrality and 40°–41°C in those adapted to cold. In the rats adapted to 36 °C we did not observe any effect of noradrenaline. Our findings concerning the effect of noradrenaline in the first 2 groups of rats are similar to those reported by JANSKY at al.[1] on the rat kept at 25 °C, but the rise in heat production found under our experimental conditions was higher. This difference may be explained by the higher dose of the noradrenaline applied. The rise in heat production in our experiments was smaller in comparison with that reported by HOŠEK and NOVAK[3] for mice, but the duration of the effect was longer. The mortality in our groups of rats adapted to cold was about 40%, occurring a few days after the experiment, but no cases of death were observed in the rats adapted to 30 °C or to 36 °C.

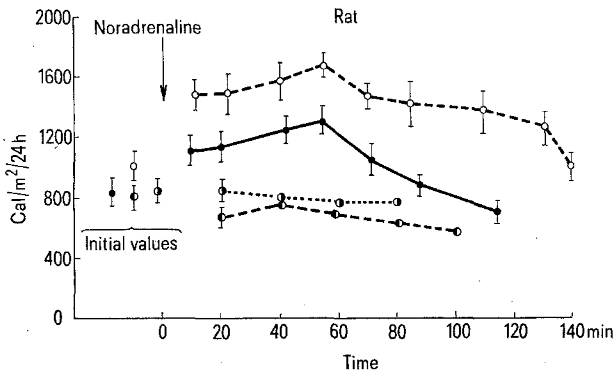

Fig. 1. The effect of noradrenaline (1.6 mg/kg) on the heat production in the rat: ○--○, adapted to 4 °C; ●—●, adapted to 30 °C; ◐--◐, adapted to 36 °C; ◑--◑, controls (physiological solution).

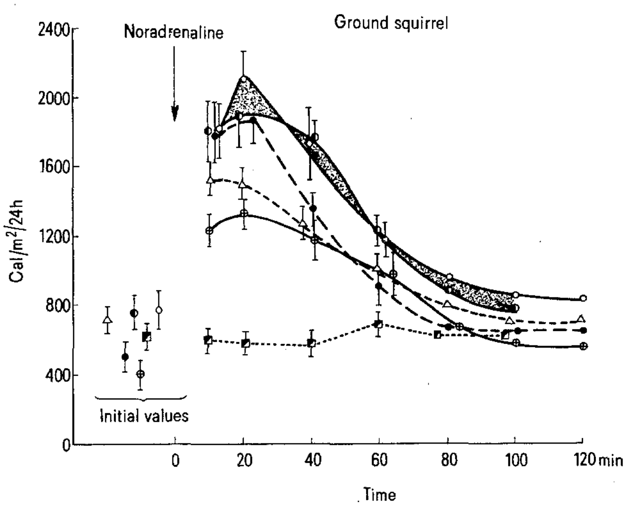

Fig. 2. The effect of noradrenaline (1.6 mg/kg) on the heat production in the ground squirrel. Active examined in October: ●--●, adapted to 30 °C; ⊕—⊕, adapted to 36 °C. After artificial arousal from hibernation: ◐—◐, examined in October; ○—○, examined in February-March. Active examined in May–June: △—△, adapted to 25–30 °C; ◧---◧, controls (physiological solution). Data for the active animals, aroused from hibernation and examined in February–March, and for active one adapted to 20–25° and examined in May–June taken from PETROVIĆ et al.[6].

In all groups of ground squirrels, a maximal increase occurs 10 to 20 min after the injection, with a tendency to decrease very quickly, but the complete restoration of the initial values occurred about 80 min after the injection. The highest level of heat production was found in animals artificially aroused from hibernation and in active animals adapted to 30 °C (both examined in October). Significantly lower values were found in the animals adapted to 36 °C and examined in October. It should be pointed out that the initial values of heat production (registered before the injection) were lower in the active animals examined in October than in artificially aroused ones. Thus, the precentage of the increase over initial values was 245% for animals adapted to 30 °C, 225% for those adapted to 36 °C and 130% for animals aroused from hibernation. In the control group there was no difference in the heat production before and after the injection of physiological solution. Under the influence of noradrenaline the body temperature in all groups of ground squirrels increased, reaching 39° to 40 °C, but no case of death was observed.

Conclusion. The capacity for heat production under the influence of the same amount of noradrenaline is significantly higher in the ground squirrel than in the rat, adapted to the same environmental temperatures. In the ground squirrel adapted to heat (36 °C), in contrary to the rat, there is a high sensitivity to noradrenaline. If we take into consideration the association between the response to noradrenaline and the extent of non-shivering heat production, demonstrated in guinea-pigs[9], the capacity of non-shivering thermogenesis in the ground squirrel is higher as compared with that in the rat. In addition, the adaptation to extreme heat (36 °C) did not reduce the capacity of nonshivering thermogenesis in the ground squirrel as it did in the rat, as evaluated by the sensitivity to injected noradrenaline. This should be correlated with the capability of the ground squirrel to respond immediately, by increasing heat production, to the aggression of low external temperature.

Résumé. La capacité de produire de la chaleur sous l'influence de la même quantité de noradrénaline est beaucoup plus élevée chez le Spermophile que chez le rat. D'autre part, le séjour prolongé à la température de 36 °C – contrairement à ce qui se passe chez les rats – ne réduit pas la sensibilité à la noradrénaline chez les Spermophiles examinés en octobre.

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