and S_i or m (from equation 4) as a function of t. Figure 1a shows the result of 2 experiments with glycerol in a double reciprocal plot of v versus S_i according to Lineweaver and Burk[2]. The abscissa intercept is near zero (as predicted) with a value of −0.009. The plot of 1/v versus 1/m (figure 2b), however, yields a negative abscissa intercept of −1.027 and gives a k_m-value of 0.974.

The evaluation according to Lineweaver and Burk requires the estimation of slopes, which decreases the accuracy. Therefore, 2 series of experiments were evaluated with the use of integrated equations. Equation 1a can, for the condition V = 1, be written

$$-\frac{dt}{dm} = \frac{1}{v_{max}}\left(1 + \frac{k_m}{m}\right) \tag{1b}$$

and integrated to give

$$\frac{t}{m_o - m_t} = \frac{1}{v_{max}} + \frac{k_m}{v_{max}} \cdot \frac{\ln (m_o/m_t)}{m_o - m_t} \tag{6}$$

which is formally similar to equation 1a, but can be used without estimating slopes. Figure 2 gives the results of a series of 6 experiments with glycerol at 37 °C evaluated using equation 6. A value of 0.980 ± 0.137 is obtained for the negative abscissa intercept. A similar series of 6 experiments with ethylenglycol at 20 °C yielded a negative intercept of 1.095 ± 0.26. Thus, the prediction made above in the discussion ef equation 5 is well substantiated. If the system under consideration actually is carrier-mediated, with a true Michaelis constant of k_m, then the apparent value of k_m (denoted as 'k_m') as obtained from a double reciprocal plot of 1/v vs 1/m will be lower than true k_m, indicating a false (too light) value for the affinity of substrate to carrier. (The error can be considerable, if the affinity is low, i.e. if k_m is high.) This emerges from substituting equation 4 into equation 1 to obtain

$$v = v_{max}\frac{(m/[m+1])\ N}{(m/[m+1])\ N + k_m} \tag{7}$$

and, in double reciprocal form (after rearranging)

$$\frac{1}{v} = \frac{1}{v_{max}}\left(1 + \frac{k_m}{N}\right) + \frac{k_m}{N\ v_{max}} \cdot \frac{1}{m}. \tag{8}$$

The abscissa intercept (which, in the Lineaver-Burk evaluation, represents $-1/k_m$), then is

$$a = -\frac{1}{'k_m'} = -\left((1 + \frac{N}{k_m}\right) \tag{9}$$

For N = 1 (e.g. isotonic saline), therefore, the value of $1/'k_m'$ is higher by 1.0 than $1/k_m$. The value of k_m, then, is

$$k_m = -\frac{N}{a+1}. \tag{10}$$

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Corticotropin and nonshivering thermogenesis

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Summary. Chronic treatment with corticotropin led to reduced calorigenic effect of norepinephrine in cold acclimatized rats, but potentiated its effect in controls. This inhibitory effect was not due to the observed decrease in corticosterone plasma level, as it was shown by metopirone administration. It is concluded that corticotropin could have a competitive action on receptor sites mediating the calorigenic effect of norepinephrine in nonshivering thermogenesis.

The occurrence of nonshivering thermogenesis (NST) in constant or fluctuating cold-acclimatised rats is related to a hypersensitivity to calorigenic effects of norepinephrine (NE)[2]. In these animals, the increase in calorigenic effect of NA may be related to an increase in lipolytic effect of NE[3,4]. Corticotropin is also known to have a lipolytic action in vivo[5] and in vitro[6,7].

The aim of this investigation was to study the dependence of NE calorigenic effect on corticotropin or corticosterone in rats acclimatized to different temperatures.

Materials and methods. Experiments were performed on Long-Evans male rats. Animals were acclimatized for 2 months to different thermic conditions: a control group was maintained at 28 °C (thermal neutrality), another group was acclimatized to a constant cold at 5 °C (CA). The last group was acclimatized to a nycthemeral fluctuating temperature from 5 °C to 28 °C (Cy). The enhancement of oxygen consumption by NE infusion (4 µg/kg during 15 min) was used as an estimation of NST[8]. Oxygen consumption ($\dot{V}O_2$) was measured at 25 °C using a Beckman analyzer. Infusions of NE were performed through the jugular vein on unanesthetized and unrestrained rats. Several days before experiments, jugular vein was catheterized. Plasma and adrenal corticosterone levels were estimated using fluorometric method of Silber et al.[9].

Results and discussion. When given by acute injection (10–20 IU/kg i.v. or i.p.) or infusions (5 IU/kg during 15 min), no effect of corticotropin (ACTH, Choay) on $\dot{V}O_2$ or on calorigenic effect of NE were observed. Chronic administration (2 IU/kg for 10 days) led to an increase in basal metabolism (20%) and calorigenic effect of NE (50%) in controls (table). In Cy group, basal metabolism was increased (25%) but calorigenic effect of NE was not changed. In CA group, basal metabolism was not changed, but calorigenic effect of NE was decreased (40%).

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Effect of corticotropin and metopirone treatment on corticosterone production and on calorigenic response to norepinephrine infusions

Acclimatisation		Saline	Corticotropin	Metopirone[a] A	Metopirone[a] B
Controls	Corticosterone (μg/100 ml/plasma)	30.5 ± 3.2 (16)	36.5 ± 9.3 (9)	14.2 ± 1.3 (10)*	28.6 ± 4.2 (9)
	μg/g adrenals	39.0 ± 3.1 (8)	38.7 ± 11.3 (8)	9.3 ± 1.6 (9)*	23.2 ± 4.8 (9)*
	Increase in VO_2[b] (%)	44 ± 3 (19)	67 ± 6 (7)*	53 ± 5 (10)	41 ± 7 (10)
Cy group	Corticosterone (μg/100 ml/plasma)	42.6 ± 3.4 (21)	36.5 ± 9.3 (9)	17.2 ± 2.2 (10)*	31.6 ± 3.8 (11)
	μg/g adrenals	29.5 ± 4.4 (9)	38.7 ± 11.3 (8)	7.6 ± 0.8 (9)*	32.0 ± 3.9 (9)
	Increase in VO_2 (%)	87 ± 3 (17)	74 ± 7 (8)	98 ± 8 (10)	59 ± 4 (10)*
CA group	Corticosterone μg/100 ml/plasma	45.0 ± 2.5 (18)	29.9 ± 4.4 (11)*	20.3 ± 2.3 (10)*	26.4 ± 4.7 (9)*
	μg/g adrenals	36.1 ± 5.3 (11)	15.3 ± 2.6 (9)*	7.3 ± 1.5 (8)*	36.8 ± 5.3 (7)
	Increase in VO_2 (%)	100 ± 6 (14)	61 ± 8 (10)*	134 ± 10 (9)*	55 ± 8 (11)*

[a] The measurements were performed: *A* 1 h, *B* 24 h following metopirone administration. [b] Enhancement of O_2 consumption following a 15 min infusion of norepinephrine (4 μg/kg). * Significant differences ($p < 0.05$) with saline-treated animals. Between brackets: number of experiments.

2 possibilities could explain the enhancement of calorigenic effect of NE by corticotropin treatment in controls: a direct effect of the hormone as it was observed in the brown adipose tissue of young rats[10] and rabbits[11]; or an indirect effect via corticosterone production with potentiation of calorigenic effect of NE as it was shown on epinephrine effect in vitro[12]. In control and Cy groups, chronic treatment with ACTH did not significantly change plasma and adrenals corticosterone levels (table). These results agree with Holzbauer[13]. On the contrary, in CA rats, plasma and adrenals corticosterone levels were decreased. So, in these animals, there was a parallel decrease in corticosterone and in calorigenic effect of NE suggesting a possible relation between corticosterone plasma levels and calorigenic effect of NE.

The production of corticosterone is modified by metopirone administration. It is known[14] that this product inhibits corticosterone production during the 3 h following administration. Then, there is an increase in hormonal production via a feedback control of corticotropin production. In this experiment, metopirone (Ciba) was administrated (100 mg/kg i.p.) either by single injection 1 h before measurements, or by 2 injections 18 and 24 h before experimentation. At 1 h, large decreases in plasma and adrenals corticosterone levels were found in all groups (table). In control and Cy groups, the calorigenic effect of NE was not affected; in CA group, it was significantly enhanced (table). At 24 h, the metopirone-dependent increase in corticotropin production[14] did not change corticosterone plasma levels. However, in CA and Cy groups there was a decrease of calorigenic effect of NE. These results support the conclusion that calorigenic effect of NE is independent of corticosterone production. So, the observed action of corticotropin treatment on NE calorigenic effect could be produced at the cellular level. Calorigenic effect of NE is due to a stimulation of receptors as shown by the effect of propranolol, adrenergic blocking agent; however, the blocking effect of that agent is more important in cold-adapted rats[2]. The lipolytic effect of corticotropin is, in some cases, blocked by propranolol but it seems that this substance does not react with the same receptor sites as catecholamines[15,16]. In control rats, this fact could explain the potentiation of NE calorigenic effect by corticotropin chronic administration. But, in cold acclimatized rats, it seems that the effects of the 2 substances are competitive. Possibly, cold acclimatization leads to a modification of hormone receptors in some calorigenic tissues, such as brown adipose tissue. A similar effect was observed in such tissue for the hormonal stimulation of adenylate cyclase[17]. Further investigations are necessary to elucidate this phenomenon.

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Does the long term wear of contact lenses produce a loss of corneal sensitivity?

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Summary: Corneal sensitivity was measured with the Cochet-Bonnet aesthesiometer in a control group of 42 people and in 82 people who had worn hard contact lenses for various amounts of years. Corneal sensitivity was found to diminish significantly after a few years of wear, thus placing the wearer at some risk.

It is known that wearing hard contact lenses which are impermeable to oxygen gives rise to some oxygen deprivation[1,2] in spite of the flow of tears behind the lens at each blink. After many years of contact lens wear this deprivation may produce marked changes in the sensitivity of the cornea, since these always accompany any changes in corneal metabolism. This study reports measurements of corneal sensitivity in people who have worn contact lenses for various durations and compares these measurements with those obtained in people who have never worn contact lenses.

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