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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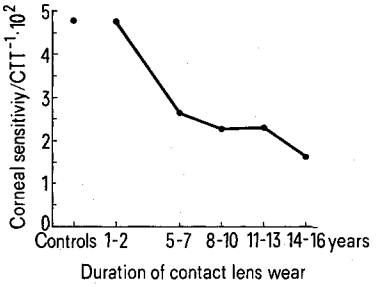
Material and methods. The cornea was stimulated by the Cochet-Bonnet aesthesiometer[3]. The instrument consists of a nylon monofilament of 0.12 mm diameter which can produce pressures ranging from 11–200 mg/0.0113 mm^2. The aesthesiometer was mounted in a holder so that it could be moved in x, y and z planes by means of 3 knobs. Thus it was possible to achieve reliability in stimulation of the same corneal point, a steady speed of application and a perpendicular corneal contact. A corneal point near the lower limbus was stimulated and the slightest bend of the nylon wire was defined as corneal contact whilst the subject fixated a target in front and above him. The peripheral corneal point was chosen because the touch threshold measured there is usually unaffected by apprehension factors[4] and because it is affected by contact lens wear to a similar extent as the centre of the cornea[5]. Measurements of corneal touch threshold (CTT) were made subjectively[6]. The experiment began with stimulation of the cornea with the lowest pressure and continued in an ascending fashion. At each predetermined length of the monofilament (with increments equal to 0.5 cm) 4–6 contacts were made with at least 1 blank to test the subject's reliability. The subject indicated when he felt the probe by pressing a bell. From these measurements CTT was defined as the length of the monofilament at which the subject responded for 50% of the number of stimulations. This length was converted into pressure using a previously calibrated curve for the instrument. All measurements were taken when the humidity in the room ranged between 50 and 60% because the nylon monofilament is affected by humidity.

The subjects were divided into two groups: the control group (42) 21–30 years old; the experimental group (82) 21–46 years old, consisted of people who had worn hard contact lenses for various durations (1–16 years). All were perfectly adapted to their lenses, free of any problems and wore them at least 12 h every day. These lenses had been fitted by various practitioners, mostly outside the university. All subjects were tested between 9 and 11.30 h. All contact lens wearers were instructed to report to the laboratory without having worn their lenses since the previous evening. The experimenter was unaware of the duration of wear of the contact lenses of most subjects until after the results.

Corneal touch threshold (mg · mm^{-2}) in the control group and in people who have worn hard contact lenses for various lengths of time

	Controls	Duration of contact lens wear (years)				
		1–2	5–7	8–10	11–13	14–16
No. of subjects	42	15	25	14	20	8
Mean	21.3	22.7	43.3	47.5	46.1	64.5
SD	13.9	7.2	15.3	12.7	11.9	12



Relationship between the length of wear of hard contact lenses and corneal sensitivity. Corneal sensitivity is the reciprocal of the corneal touch threshold (CTT) measured in mg · mm^{-2}. Each data point represents the mean corneal sensitivity of the number of subjects tested in each group.

Results and discussion. The results are given in the table. The threshold values for each subject were converted into sensitivity (CTT^{-1}) and are plotted in the figure. The spread of the results of the control data confirm previous measurements[6]. It is mainly attributable to differences in eye colour[7] and inherent biological differences. The variability of the findings of the contact lens wearers can, in addition, be accounted for by several other factors. First the type of fit of the contact lenses may vary slightly and consequently the metabolism may be variably affected[8]. Second, the exact number of hours of wear per day may influence the results as it has already been shown that this is directly related to the loss of sensitivity within a day[5].

As shown in the figure, corneal sensitivity is practically the same after 1–2 years as it is in the control group ($p > 0.2$). This is probably due to the fact that these people recover fully after some 12 h without their lenses. However, after 5–7 years of wear, corneal sensitivity has diminished significantly as compared to the control group ($p < 0.001$) being, on average 103% lower. It continues to decrease slightly as the length of wear increases but the exact rate of decline remains to be established with more measurements. This loss of corneal sensitivity caused by the wear of hard contact lenses is further corroborated by 2 other observations. In one case, corneal sensitivity was measured 9 years ago when the person had worn contact lenses for only 3 years and CTT was found to be 36 mg mm^{-2} whereas after 12 years it has now risen to 63 mg mm^{-2} (i.e. 75% lower corneal sensitivity). The other observation was provided by 2 persons both of whom had worn only 1 contact lens for 11 years (the other eye being perfectly healthy and emmetropic). Both were found to have lower sensitivity in the eye which had worn the contact lens than in the other eye by 95 and 46%, respectively.

It could be argued that the reduced corneal sensitivity exhibited by the people who have worn their lenses the longest could be attributable to the fact that these people are somewhat older than the others. Although corneal sensitivity does indeed diminish with age[9], it does so by only a small amount up to 50 years old, that is far less than the loss displayed by long term contact lens wearers.

This phenomenon may explain why contact lens patients feel more comfortable as time goes on. They are slowly losing their natural warning mechanism which is the essence of the exquisite sensitivity of the cornea, indeed the most sensitive part of the body[10]. Thus hard contact lens wearers of many years standing could be at greater risk of corneal infection occurring without their being aware of it. Obviously, the lesion would be felt eventually but much later than in someone who does not wear contact lenses.

It has been reported that hard contact lenses produce oxygen deprivation which may be of sufficient severity to interfere with corneal metabolism[1,2]. However, the mechanism which leads to a decrease in corneal sensitivity is, as yet, unknown. It will also be important to elucidate whether the loss of corneal sensitivity with hard contact lens is a reversible process.

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