EFFECT OF COLD-EXPOSURE ON SERUM THYROTROPHIN LEVELS IN MAN

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ABSTRACT

Serum TSH levels were measured after exposing male volunteers to cold, or successively to warmth and to cold, causing clear changes in body temperature. Very moderately heated Finnish sauna bath increased body temperature to about an average of 39°C, and cooling in a relatively warm swimming pool (+25 to +28°C, 30 min) decreased body temperature to below 35°C after sauna, and to about 33°C without sauna. In both cases a slight but significant initial increase of serum TSH was demonstrated. No changes in serum T₃ or ETR were seen. The results suggest that a similar mechanism of initial TSH response may exist in humans as has previously been demonstrated in rats.

There is increasing evidence that the pituitary-thyroid axis can be activated by cold-exposure both in subacute (Uotila 1939) and in short-term experiments (Itoh et al. 1966; Tuomisto et al. 1973, 1975; Kajihara et al. 1972; Kotani et al. 1973; Leppäluoto et al. 1974) in animals. The initial temporary increase is very fast and relatively brief (Itoh et al. 1966; Leppälauoto et al. 1974). This response seems to be centrally regulated by hypothalamic neuroendocrine mechanisms and can be blocked both by brain lesions (Kajihara et al. 1972) and by centrally acting drugs (Kotani et al. 1973; Tuomisto et al. 1973, 1975).

There is much less unanimous agreement as to the existence of a similar mechanism in humans. Fisher & Odell (1969) and Wilber & Baum (1970) de-
monstrated that the cooling of infants provokes TSH release, and Golstein-Golaire et al. (1970) found a similar response in adults at some time points. However, other reports on adults have been negative (Berg et al. 1966; Hershman et al. 1970; Fisher & Odell 1971; Woolf et al. 1972). In none of these negative reports is there convincing evidence of a marked lowering of body temperature in adults, although such a decrease was clearly seen in the animal experiments (Tuomisto et al. 1975) and also in the studies on infants cooled for cardiovascular surgery (Wilber & Baum 1970). Therefore, a more effective cooling, or cooling combined with heating in the Finnish sauna bath, was tested to study the influence of changes in body temperature on TSH secretion.

MATERIAL AND METHODS

This study was done on three occasions, in June, in September and in November. The subjects were seven healthy male physicians, age 24 to 34 years and weights 62 to 80 kg. Two kinds of experiments were performed, partially in a cross-over fashion (four of the volunteers took part in both experiments). In one experiment, the subjects were 30 min in a swimming pool (+25 to +28°C) trying not to swim and to move about as little as possible. In the other experiment, the subjects were at first 30 min in the Finnish sauna (+55 to +60°C, dry atmosphere) and then 30 min in the pool as above. After having been in the pool the subjects dried and dressed themselves. The oral temperature was measured from the soft palatine every tenth minute with a one-minute thermometer (b 128 Max. Labortherm N). Cubital vein blood samples were drawn before the experiment, after the sauna, after the immersion and thereafter as indicated. Radioimmunoassay techniques were used for the determination of serum TSH (Gordin & Saarinen 1972) (normal range 1.6–6.9 mU/l), and triiodothyronine (Amersham T3-RIA Kit, range 1.50–2.90 nmol/l). The effective thyroxine ratio (ETR) was determined according to Liewendahl & Helenius (1975) (range 0.86–1.14). The sera were stored at −18°C until analyzed. All samples belonging to the same experiment were analyzed simultaneously. Means ± SEM were calculated and Student’s t-test for paired samples was used for calculating the significances between the means.

RESULTS

Cold exposure alone

The oral temperature rapidly decreased in the pool to about 34.5°C, but reached the minimum only after the cooling period (Fig. 1). The minimum temperature was about 33°C on an average. This may be slightly inaccurate, because in some cases the lowest limit of the thermometer was reached. The normal range of body temperature was re-attained relatively slowly, in about two hours or more.

There was a significant increase in serum TSH after the cooling period, as compared to the pre-cooling level (at 60 min < P 0.01, Fig. 1). The level did
Body temperature and serum TSH in five male volunteers subjected to cooling in a swimming pool at +25 to +28°C for 30 min. Means ± SEM.

not increase further in later samples, although there was a fluctuating trend. The values measured in two and three hour samples were not different from the pre-cooling level. No changes in ETR and T₃ levels were seen (Table 1).

**Successive warm and cold exposure**

In the sauna the body temperature increased to 39.0 ± 0.08°C at the end of the 30 min period. In the pool, there was a very abrupt decrease to about 35°C, and again the minimum body temperature was reached, only after the

Body temperature and serum TSH in seven male volunteers subjected first to heating in the Finnish sauna at 55–60°C and then to cooling in a swimming pool at +25 to +28°C for 30 min each. Means ± SEM.
cooling period when the subjects were already fully dressed. However, the temperature did not decrease quite as much as without sauna.

TSH was slightly and not significantly decreased after sauna, and increased significantly after cooling in the pool ($P < 0.05$). It returned to the initial level in another 30 min. In two subjects there was a secondary increase 4 hours after the cooling. No changes in ETR were found.

DISCUSSION

In the present experiments a fast and transient increase in serum TSH levels was found after cooling healthy human volunteers in a swimming pool. The response was approximately the same, regardless of the preheating period in the sauna. The increase is similar in timing to that observed in rats exposed to $+4 \degree C$ room temperature, but in the present experiment the increase was much smaller. In addition to possible species differences there may be several reasons for this. Even in rats the response was quite unreliable unless the animals were adapted to a temperature of $+30 \degree C$ for at least one week (Tuomisto et al. 1975; Kotani et al. 1973). In humans this kind of adaptation is obviously very difficult to carry out. As an alternative, a short heating period was used in this study to reveal possible inhibitory mechanisms and to decrease the basal level of TSH. However, no clear difference was seen between the groups. The decrease in body temperature in this study was significant although slower than that seen in rats (Tuomisto et al. 1975). Too slight a change has possibly been one reason for the failure to detect any effects in most earlier studies.
In those a decrease of about 0.5°C (Berg et al. 1966; Fisher & Odell 1971) to about 1.5°C (Hershman et al. 1970) was seen. In the present study a relatively effective cooling medium was chosen, but too cold water was avoided in order to minimize the shivering and subjective discomfort which might prevent the decrease in body temperature.

These results resemble those of Golstein-Golaire et al. (1970) although the initial increase in TSH at 30 min was not significant in their experiments, possibly due to a different cooling procedure (2 h in a cold room at +4°C). However, also in their data there is a trend towards an increase at 30 min, and then a significant sustained increase after 2–6 h. The later response was seen only in a few subjects in this study.

It is possible that the initial response is due to an adrenergically mediated TRH release which has been suggested as operating in rats (Tuomisto et al. 1975; Grimm & Reichlin 1973). Due to the slight increase in humans and to the difficulty of selectively and effectively blocking the adrenergic receptors in the human central nervous system, this may be somewhat difficult to prove directly. The later increase may have another mechanism, and various possibilities have been discussed (Golstein-Golaire et al. 1970). In any case it seems obvious that the increase is not due to the increased utilization of peripheral hormones and to the subsequent compensatory TSH response, since no changes in serum T₃ or ETR levels were found.

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