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THERMOREGULATORY RESPONSES AS A FUNCTION OF CORE TEMPERATURE IN HUMANS

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SUMMARY

1. Six healthy humans were immersed sequentially in baths maintained at a steady temperature of either 28 ± 1 or $38{\cdot}8 \pm 1°$ C.

2. Metabolic heat production was calculated by respiratory gas analysis. A ventilated capsule was placed on the forehead and sweat secretion was calculated from psychrometric recordings. Convective heat loss from one hand to a water-perfused glove provided a continuous measurement of vasomotor response.

3. Heat production, sweating, and vasomotor heat loss were proportional to core temperature.

4. Sweating and vasomotor response were parallel. Vasoconstriction was complete, before the onset of shivering.

5. The thresholds for heat loss and heat production were superimposed, without a 'dead band' core temperature.

INTRODUCTION

The 'upper critical temperature' is the ambient temperature above which thermoregulatory evaporative heat loss processes of a resting thermoregulating animal are recruited (Bligh & Johnson, 1973). The 'lower critical temperature' is the ambient temperature below which the rate of metabolic heat production of a resting thermoregulating animal increases by shivering and/or non-shivering thermogenic process to maintain thermal balance (Bligh & Johnson, 1973). The 'thermoneutral zone' is situated between these two critical temperatures; it is defined as the range of ambient temperature within which metabolic rate is at a minimum, and within which temperature regulation is achieved by non-evaporative physical processes alone (Bligh & Johnson, 1973). This notion of a thermoneutral zone is generally admitted, although Hardy & Dubois (1938) showed

that, in humans, thermal neutrality is limited to a narrow zone around 29° C. On their respective sides of this zone, thermogenesis and thermolysis are proportional to the environmental stress. When, following Hammel, Jackson, Stolwijk, Hardy & Strømme (1963), physiologists began to express the magnitude of thermoregulatory responses, not as a function of ambient temperature, but as a function of core temperature, they also found that these responses were proportional to core temperature. This was true for heat production (Hellestrøm & Hammel, 1967; Benzinger, 1970; Jessen & Mayer, 1971; Jessen & Simon, 1971), for evaporation water loss in humans (Henane & Bittel, 1975; Henane & Valatx, 1973; Benzinger, Kitzinger & Pratt, 1963; Nadel & Stolwijk, 1973; Wyss, Brengelmann, Johnson, Rowell & Niederberger, 1974), and for peripheral blood flow in humans (Wyss, Brengelmann, Johnson, Rowell & Silverstein, 1975; Wenger, Roberts, Stolwijk & Nadel, 1975*b*; Wenger, Roberts, Nadel & Stolwijk, 1975*a*). Strangely enough, experiments were always limited to the study of responses either to high or to low environmental temperatures but not to both. Therefore, when theoretical models were proposed with core temperature as abscissa, they naturally included a dead band (Bligh, 1972; Hammel, 1965). In contradiction to these theoretical models, Jessen & Clough (1973), studying temperature regulation in the goat, demonstrated a continuity of thermogenesis and evaporative heat loss when expressed as functions of core temperature. Thus the goat does not seem to have a dead band in the control of its core temperature; such a dead band would be equivalent to a 'neutral thermal zone' of core temperature.

It seemed, therefore, interesting to look for the presence of a dead band or core neutral thermal zone in humans. In addition, peripheral vasomotor tone, the third major thermoregulatory response, is supposed to come into action between shivering and evaporative heat loss and to be the only 'dead band' response; it was necessary, therefore, to measure it in addition to shivering and sweating.

METHODS

Six healthy male human subjects were immersed in warm water (38·8 ± 0·8° C) on twenty-six occasions and in cool water (28 ± 1° C) on thirteen occasions. The nude subjects were immersed up to their necks in a well stirred thermostated bath tub.

Measurements. Each subject's left hand was immersed in a glove, outside the bath, perfused with a constant flow (800 ml. min^{-1}) of water at a constant (20° C) temperature. Temperature difference between inflowing and outflowing water was recorded and compared to a control without the hand. This direct calorimetry of the hand reflected local blood flow, as a negligible amount of heat was being produced by the tissues of the hand. An example of such a recording is given in Fig. 1. A capsule (8 cm^2) was attached to the subject's forehead. The capsule was ventilated by dry air at a constant flow of about 8 l. min^{-1}, in order to maintain dryness of the skin

beneath the capsule. The air leaving the capsule passed over the two thermocouples of a psychrometer. The psychrometer was calibrated against a high precision perfusion pump. Evaporative heat loss was calculated from the psychrometric recordings and from air flow, for 2 min periods. Fig. 1 shows such a result. Metabolic heat production was calculated from respiratory measurements. Every minute, expiratory air flow and oxygen content were measured on 30 sec air samples. When core temperature quickly changed, 30 sec samples were taken without interruption. There was no lag between shivering (observed by the experimenters or experienced by the subjects) and increase in oxygen consumption. In addition to the above recordings, oesophageal (core) temperature (T_{es}) and bath temperature were recorded.

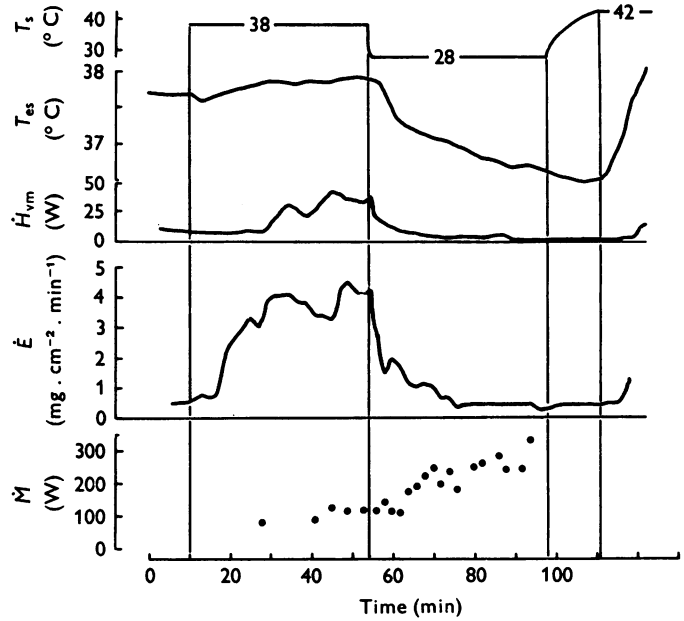

Fig. 1. One example of recordings and experimental sequence for one subject. T_s, bath temperature; T_{es}, oesophageal temperature; H_{vm}, heat lost from left hand to glove; E, water evaporated from forehead under 8 cm^2 capsule; M, metabolic heat production.

Experimental sequence. An example of the experimental protocol is given in Fig. 1. Oesophageal and bath thermocouples, as well as the capsule with thermocouples, were positioned, and the subject was then immersed in the warm bath. Each experiment included a sequence of three conditions: the first bath was warm and lasted until the subject was clearly hyperthermic, sweating, and vasodilated; the second bath, cool, was produced by sudden addition of ice and lasted until the subject was clearly hypothermic, shivering, and vasoconstricted; the bath water temperature was rapidly increased again, until sweating and vasodilatation were visible on the recordings, i.e. until the thresholds for these variables could be clearly detected. The durations of each bath were different from subject to subject because of different speeds of T_{es} change due to different physical characteristics and especially skin adiposity.

Calculations. The recordings were analysed by averaging the results of 2 min periods. Then, the responses, including metabolic heat production, evaporative capsule water loss, and left hand vasomotor heat exchange, were plotted against oesophageal temperature. An example of the results obtained in a cool bath is shown in Fig. 2. Each of the three autonomic responses exhibited a minimum value, at high T_{es} for metabolic heat production; at low T_{es} for vasomotor heat loss and sweating. These minimum values were easily identified in all experiments. They will be referred

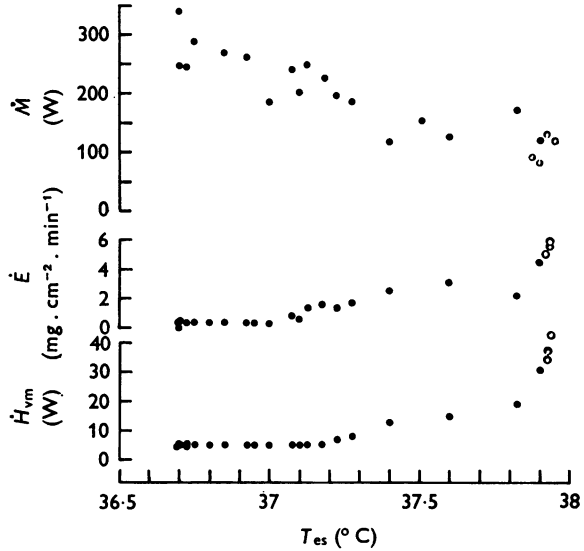

Fig. 2. One example of plotting of results against oesophageal temperature in a cool (28° C) bath. The results plotted here are those of Fig. 1. M, metabolic heat production; E, water evaporated under forehead capsule; H_{vm}, heat lost from left hand to glove; the three open circles are the last of the warm bath and the first of the cool bath. Each dot represents a period of 2 min.

to as 'minimal response' in the following text. All results expressed are the average results for all experiments. Two other elements were averaged in the same way: (i) the threshold oesophageal temperatures were readily detectable on the records as the points at which each of the three responses started to rise above the minimum response level; (ii) the slope of the regulatory responses. Both of these elements were obtained from the regression lines of the responses plotted against T_{es}. Mean values and error statistics reported below are related to the number of subjects in order to minimize the fact that not all subjects had the same number of trials. Nevertheless, means, related to the number of trials, produced superimposed figures.

RESULTS

Results are the average minimal responses, thresholds, and slopes presented by the three main responses. All results are expressed in Table 1. They were analysed separately for cold baths and warm baths.

TABLE 1. Mean values of minimal responses, threshold-T_{es} and magnitude of thermoregulatory responses for the six subjects in a warm and a cold bath

	Sweating	Vasomotor response	Heat production
Cool bath			
Minimal response	$0{\cdot}8 \pm 0{\cdot}1$ mg.cm^{-2}.min^{-1}	$8{\cdot}8 \pm 1{\cdot}8$ W	148 ± 22 W
Threshold (° C T_{es})	$37{\cdot}32 \pm 0{\cdot}06$° C	$37{\cdot}30 \pm 0{\cdot}07$° C	$37{\cdot}34 \pm 0{\cdot}07$° C
Slope	$5{\cdot}90 \pm 2{\cdot}6$ mg.cm^{-2}.min^{-1}.° C^{-1}	$54{\cdot}00 \pm 16{\cdot}90$ W.° C^{-1}	$-1182{\cdot}8 \pm 148$ W.° C^{-1}
Warm bath			
Minimal response	$0{\cdot}9 \pm 0{\cdot}2$ mg.cm^{-2}.min^{-1}	$9{\cdot}2 \pm 1{\cdot}2$ W	
Threshold (° C T_{es})	$37{\cdot}38 \pm 0{\cdot}04$° C	$37{\cdot}35 \pm 0{\cdot}05$° C	
Slope	$7{\cdot}6 \pm 2{\cdot}2$ mg.cm^{-2}.min^{-1}.° C^{-1}	$158{\cdot}8 \pm 36$ W.° C^{-1}	

1. *Thermoregulatory responses in the cool bath*

The results are summarized in Table 1 and Fig. 3. The trend in such a bath was from hyperthermia toward hypothermia.

Metabolism. In hyperthermia, the average minimal metabolism was 148 ± 22 W. This is higher than basal metabolism because the subjects were not fasting, were not at a complete rest, and were hyperthermic. Below an average threshold-T_{es}, metabolism increased proportionally to the reduced T_{es}. The average maximal metabolism was almost 4 times the resting metabolism, and was obtained for a 0·3° C decrease of T_{es} below the average threshold.

Sweating. During hyperthermia, the average maximal rate of evaporation, under the capsule, was 5·5 mg.cm^{-2}.min^{-1}. With decreasing T_{es}, the sweating rate decreased proportionally to the reduced T_{es}; it reached an average threshold. The minimal response in hypothermia was 0·83 mg.cm^{-2}.min^{-1}. This minimal evaporative heat loss was always present, even during hypothermia. This is higher than the reported values in the literature; this point will be discussed later.

Vasomotor response. This response was characterized by a slow decrease, proportional to T_{es}. An example is shown in Fig. 2. During this phase, vasomotor response strictly paralleled sweating. Hand heat loss was independent of the speed of decreasing T_{es}. Below a threshold-T_{es}, the minimal response was about 9 W.

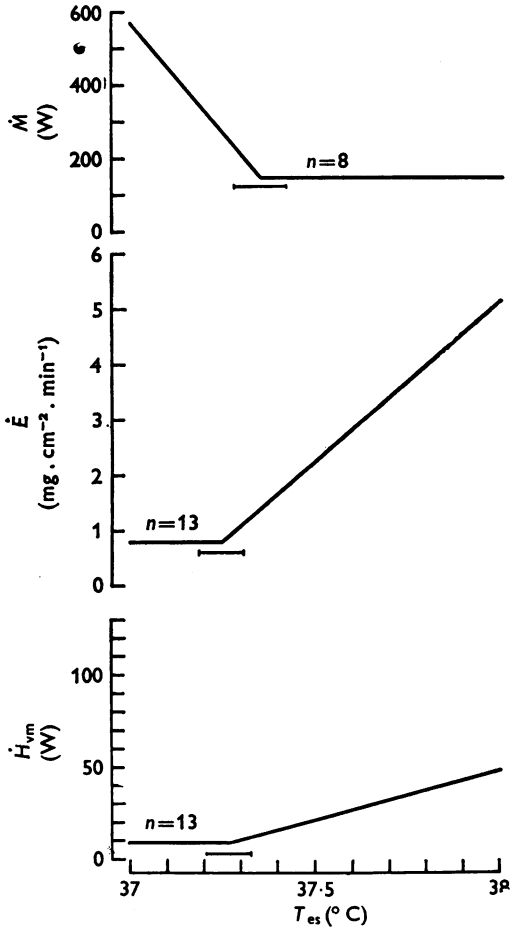

Fig. 3. Average results of experiments in cool bath. Same symbols as in Figs. 1 and 2. S.E. of the abscissae of the mean thresholds are indicated below the intersections of minimal responses and the thermoregulatory responses.

2. *Thermoregulatory responses in the warm bath*

Measurements were limited to warm defence responses and to control measurements of metabolism. In the warm bath, the subjects evolved from hypothermia to hyperthermia. The results are summarized in Table 1 and Fig. 4.

Sweating. In the warm bath, the minimal response was 0·9 mg.cm^{-2}.min^{-1} and was, therefore, identical to the minimal response in the cold bath. From a threshold-T_{es} sweat start, evaporative heat loss increased proportionally to T_{es}.

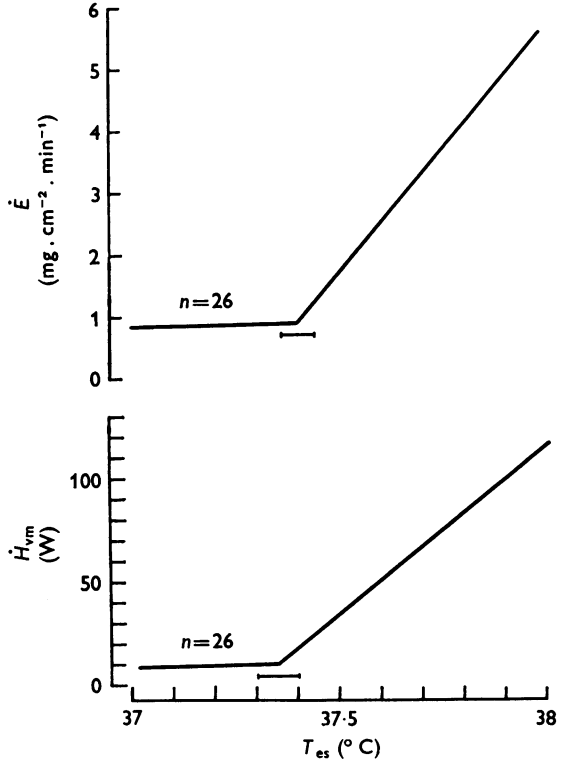

Fig. 4. Average results of experiments and S.E. on the thresholds in warm bath. Same symbols as in preceding Figures.

Vasomotor response. In the warm bath, the average minimal heat loss from the left hand to the glove was about 9 W, and was, therefore, identical to the minimal response in the cold bath. From a threshold-T_{es} vasodilation increased proportionally to T_{es}.

DISCUSSION

The above results confirm the previously observed pattern of thermoregulatory responses when plotted against T_{es}. In the condition of these experiments, there is, for each response (shivering, vasomotor tone and sweating), a minimal response, a threshold, and a proportional response. This pattern was first demonstrated in dogs (Hammel *et al.* 1963) and has subsequently been described in various other species and in humans (Wyss *et al.* 1974, 1975; Henane & Bittel, 1975; Nadel & Stolwijk, 1973; Nadel *et al.* 1974; Wenger *et al.* 1975*a*, *b*). The pattern applies to all three responses, except for the non-linear vasomotor response, which will be discussed

below. Such a pattern was obtained in all subjects, and in all experiments, independently of thermal insulation (body fat). It should be noted that in these experiments, this pattern was obtained during transient periods and the rate of change of T_{es} had no effect on the recorded responses.

In the case of shivering, the magnitude of the response and the slope are identical to those in previous experiments (Benzinger, 1970). The magnitude of evaporative heat loss is greater than that in previous experiments, at rest as well as during hyperthermia: average evaporative water loss was as great as 0·8 mg.cm^{-2}.min^{-1} at rest and as 5·5 mg.cm^{-2}.min^{-1} during hyperthermia. Two factors might explain these high values. (i) Most experiments measure entire body sweating and express it as a whole in relation to skin surface, even though large skin surfaces such as the legs are poor sweat secreters. Höfler (1968) has shown for example that the trunk sweats approximately four times more per unit area than do the legs. When the sweat capsule was placed on the knee area of a subject, the evaporative water loss was hardly higher than the basal level, while at the same moment forehead secretion was maximal. The forehead where sweating was recorded here, is probably a privileged area for sweating. (ii) It is known that the presence of sweat itself on the skin surface inhibits sweat secretion (Henane, 1972; Nadel & Stolwijk, 1973). The air flow in the capsule was adjusted to always keep the skin exposed under the capsule dry. Recorded evaporative water loss was, therefore, the maximal water transfer through the skin, at rest as well as during hyperthermia.

The magnitude of the vasomotor response estimated by the calorimetric method cannot be compared to other results based on plethysmographic methods. The caloric efficiency of vasomotor heat transfer to water is remarkable: in hyperthermia, as much as 100 W can be transferred to the glove from the hand. This amount, obtained during transient periods, is the same as that previously obtained during steady state (Cabanac, Massonnet & Belaïche, 1972). Although the proportionality of the vasomotor response is true for the warm as well as for the cool bath, the slopes are quite different. The difference in slopes is not caused by a latency of the glove method, because a delay in glove response would create a hysteresis cycle with an influence opposite to that recorded. In addition, the threshold for the vasomotor response was identical in warm and cool baths. The origin of the difference in slopes is possibly due to the multiplicative influence of mean skin temperature with core temperature, because the switch from one slope to the other occurred within 2 or 3 min, during which the bath was rapidly cooled by addition of ice (Figs. 1 and 2). This multiplicative influence of mean skin temperature with core temperature affected also evaporative water loss in several instances (e.g. Figs. 1 and 2), but on the average there was only a small and statistically non-significant

change in mean slope. Wyss *et al.* (1974) have obtained comparable results. It is, therefore, possible that skin and core temperatures affect the various warm responses according to different laws.

A careful examination of Fig. 3 and Table 1 points out another result regarding the co-ordination of the various responses. In the cool bath, the T_{es}-thresholds for sweating and for vasomotor response were not significantly different (0·02° C). In the warm bath, the T_{es} thresholds for sweating and for vasomotor response differed by only 0·03° C, a statistically and physiologically non-significant interval. The vasomotor response was always parallel to the sweating response although they were recorded in different cutaneous areas. Vasomotor response must, therefore, be regarded as a heat-resisting response: in a cool bath vasoconstriction was complete before the onset of shivering; in a warm bath vasodilatation started with the ending of shivering. During euthermia, the normal peripheral state is, therefore, vasoconstriction. This result agrees with those of Wyss *et al.* (1974).

Fig. 3 shows no interval or 'dead band' between the response of shivering and the responses of vasodilatation and sweating. This absence of 'dead band' confirms the results of Jessen & Clough (1973) on the goat, and indicates that temperature regulation is permanently active. Indeed, a slight overlap occurred between warm and cold defences and was of the order of 0·05° C. This may be considered as insignificant. Observation of affective responses to temperature stimuli leads to parallel results; there is no 'dead band' of core temperature but responses are rather either of the hyperthermic or hypothermic type, without an euthermic type (Cabanac, 1969; Cabanac *et al.* 1972). The homoeothermic organism is likely to be, therefore, permanently equilibrated between hyperthermia and hypothermia, and thermal neutrality is virtual.

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