

\* Research supported in part by a grant from the Air Force Office of Scientific Research.

<sup>1</sup> In all cases,  $\alpha$  is equivalent to the *conjunction* of  $\alpha_1, \alpha_2$ ;  $\beta$  is equivalent to the *disjunction* of  $\beta_1, \beta_2$ .

<sup>2</sup> That is, simultaneously satisfiable in a denumerable domain.

<sup>3</sup> The former states that if  $W$  is satisfiable, it is denumerably satisfiable; the latter (due to Henkin, Tarski, and Robinson) states that if every finite subset of  $W$  is satisfiable, so is  $W$ . We note that the compactness theorem for *propositional* logic results from Theorem 1.1, since truth-functional satisfiability satisfies conditions  $\Gamma_0, \Gamma_1, \Gamma_2$ .

<sup>4</sup> In the sense that the negation of the conjunction of elements of  $M$  is not provable in the system.

<sup>5</sup> Cf. Kleene, S. C., *Introduction to Metamathematics* (Princeton: D. Van Nostrand Co., Inc., 1952).

<sup>6</sup> This application was obtained in collaboration with Dana Scott.

<sup>7</sup> Craig, William, "Three uses of the Herbrand-Gentzen theorem," *J. S. L.*, 23, 3.

<sup>8</sup> For example, the ordered pair  $\langle I, M \rangle$ , where  $I$  is some new symbol.

<sup>9</sup> This is the key fact behind consistency proofs for the  $\epsilon$ -calculus, as well as natural deduction systems using existential instantiation.

<sup>10</sup> Gentzen's *erweiterter* Hauptsatz states this result (for Gentzen systems) for sets  $M$  of *prenex* formulas.

<sup>11</sup> If not, uniformly change them in  $R_1, R_2$  where necessary.

<sup>12</sup> Like Craig's system (*J. S. L.*, 23, 3) our rules are all one-premise rules; but we avoid use of prenex normal form.

<sup>13</sup> All sentences of  $M^*$  are true under the interpretation which assigns to each  $n$ -ary predicate  $P$  the set of all  $n$ -tuples  $(a_1, \dots, a_n)$  of parameters such that  $P a_1, \dots, a_n$  lies in  $M^*$ . The idea of using the set of parameters for the domain of the interpretation is due to Leon Henkin. But our construction differs essentially from that of Henkin, in that our definition of an abstract consistency property nowhere has the clause:  $\Gamma(M)$  implies  $\Gamma(M, X)$  or  $\Gamma(M, X')$ .

<sup>14</sup> It may also be of interest to note that our proof nowhere uses König's lemma on infinite trees (nor could it, since an element  $b$  may have infinitely many images  $\bar{b}$ , and a tree form of our construction might involve infinite branching).

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## PERIPHERAL COLD- AND CENTRAL WARM-RECEPTION, MAIN ORIGINS OF HUMAN THERMAL DISCOMFORT\*

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The thermostat that balances in the human body the gains and losses of energy for maintenance of constant temperature is capable of handling loads four times a normal metabolic rate. Higher intensities of thermal stress must be avoided by intelligent behavior. Wilful locomotion from one environment into another, changes of posture, immobilization or heat-producing exertion, unclothing or clothing, sheltering from heat or cold, and ultimately artificial refrigeration, air conditioning, or heating of dwellings, of working places, and of craft on land, at sea, in air, or out in space, must keep the individual gain or loss of heat far below 80 calories per second. Limited to this capacity, the more precise but weaker autonomic system will perform only when behavioral "preconditioning" prevents overloading. The main prerequisite of intelligent thermal behavior is, of course, the capacity for conscious temperature perception, which was the object of our study.

It is assumed, in general, that *skin* thermoreceptors for warm and for cold are the origins of the conscious sensations of warm or cold in man, which regulate his intelligent behavior in changing environments. Incidental experiences during work with human subjects on autonomic temperature regulation have raised our doubts that this may not be the whole truth.

In these PROCEEDINGS the autonomic, unconscious mechanisms of human temperature regulation have recently been analyzed in quantitative terms of causes and effects, stimuli and responses.<sup>1-3</sup> In warm environment, heat loss by sweating is elicited directly from a central terminal warm-sensor. (The required neurologic characteristics are found in a "center" in the anterior hypothalamus—*A* in Figure 1—discovered in 1885 by Aronsohn and Sachs.) In addition, a peripheral afferent pathway serves to inhibit sweating when, paradoxically, the skin is cooled while the center is overheated.<sup>3</sup>

In cold environment, the desired heat gain by increased metabolic action is elicited by cold-receptors of the skin. Their impulses are relayed through a synaptic, temperature-insensitive center. (The required neurologic characteristics are found in the posterior hypothalamic "heat maintenance center"—*P* in Figure 1—discovered by Isenschmidt and Krehl in 1912.) The metabolic response to cold at the skin is dramatically inhibited when central temperature rises. On animals the origin of this inhibition has been located in the anterior, not the posterior, hypothalamus (Hemingway *et al.*<sup>4</sup> and Freeman and Davis<sup>5</sup>). In conclusion, both the response to cold and the response to warm appear to be under the control of one central terminal warm-sensor. This "temperature-eye" or "human thermostat" is responsible for the maintenance of body temperature at a strictly determined "setpoint." Figure 1 shows the postulated centers, pathways, and minimum number of neurons required to explain the quantitative data of indirect and direct calorimetry. In the *autonomic* temperature regulation of man, *central* reception of warmth and *peripheral* reception of cold are dominant.

As a background for investigation of the *conscious* sensation of cold, quantitative data on the *unconscious* metabolic response to cold are interesting (Fig. 2). The inhibition of thermoregulatory heat production becomes complete when central temperature increases to the "setpoint." At this central temperature the threshold of skin temperature, where the increase of metabolism should begin, becomes infinitely low (Fig. 3). When central warm-inhibition is gradually removed by lowering of central temperature, the skin-threshold for metabolic action rises toward an extrapolated skin temperature near 35.5°C. At this threshold temperature

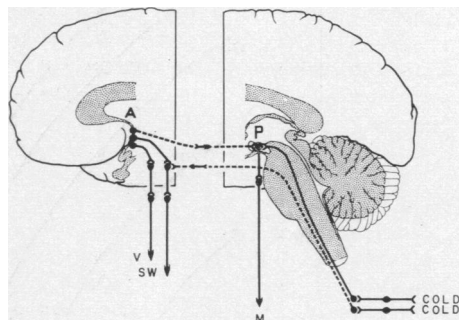


FIG. 1.—From observations with indirect and direct calorimetry, centers and pathways of autonomic temperature regulation are postulated as shown. Sweating, *SW*, and vasodilatation, *V*, are elicited from central, terminal warm-sensor, *A*. The metabolic response to cold, *M*, is driven by cold-reception at the skin, through a synaptic, temperature-insensitive center, *P*. Functions of *A* and *P*, essentially independent and different in their basic characteristics, are cross-linked only by inhibiting pathways (broken lines). Central warm-reception at *A* inhibits the metabolic response to cold. Skin cold-reception inhibits the response of sweating.

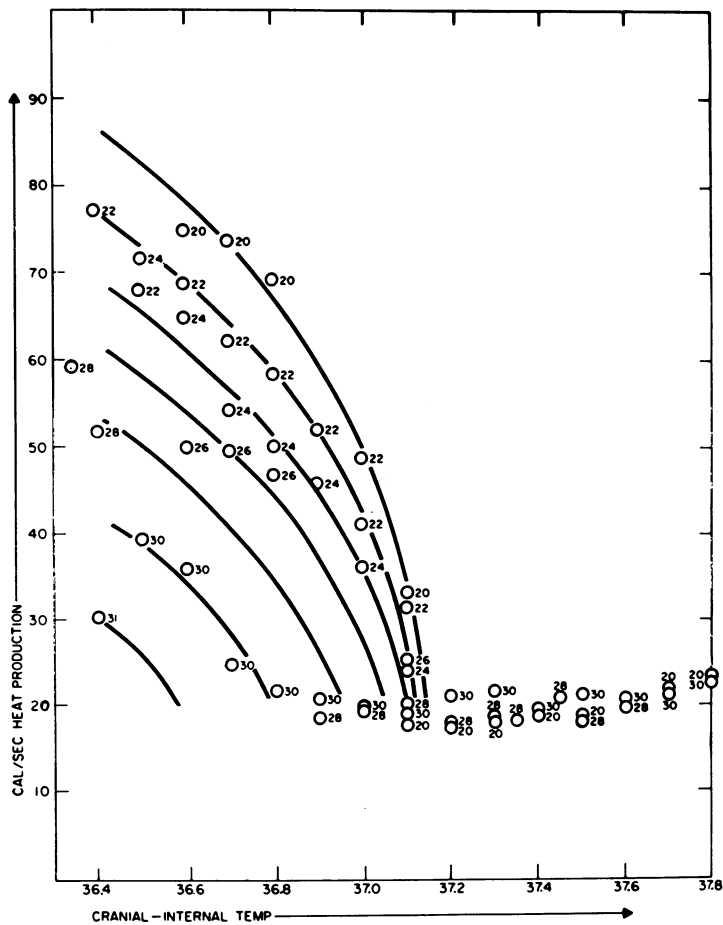


FIG. 2.—Rates of thermoregulatory heat production were plotted against tympanic temperatures. Figures indicate skin temperature. The response is maximal at 20°C and declines with increasing skin temperature (see left side of graph). With rising internal temperature toward right, the metabolic response is progressively inhibited. Inhibition becomes complete at 37.1°C, the “setpoint” of this human subject.

Hensel and Boman<sup>6</sup> find in man that cold-receptor neurons of the skin begin to fire at an increasing rate when temperature decreases. The firing rate becomes maximal,<sup>6</sup> and the response in metabolic heat production reaches a peak<sup>3</sup> when skin temperature decreases to 20°C. Likewise, near 20°C we have observed in unpublished tests a maximum of conscious cold-sensation which declines with further lowering of skin temperature. It would appear, then, that those cold-receptors of the skin that are engaged in behavioral regulation by conscious perception and those that are engaged in autonomic temperature regulation exhibit similar characteristics of threshold and maximum of activity. They also share, as common characteristics, overshooting response upon cooling and overshooting inhibition upon rewarming. One aim of our investigation was to find whether or not this analogy can be carried further. It seemed important to know whether the conscious per-

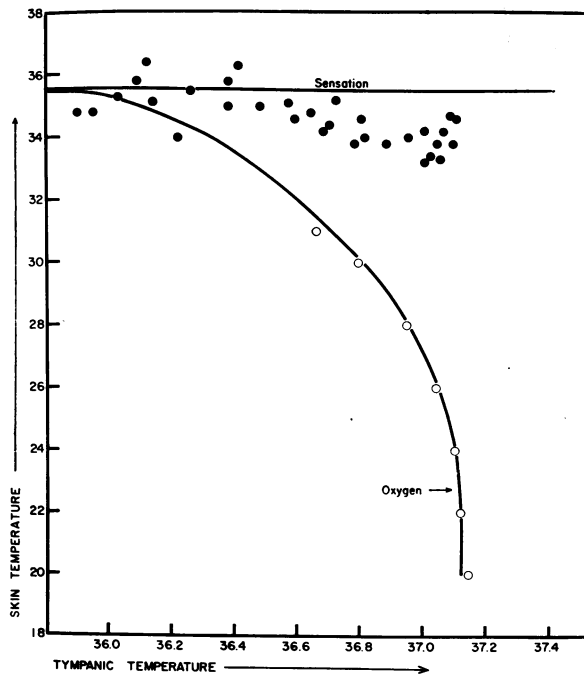


FIG. 3.—Thresholds of the beginning metabolic response from Fig. 2 were plotted against tympanic temperatures (curved line). The horizontal line with points describes threshold values of conscious cold-sensation in baths of slowly decreasing temperature with allowance for artefact. Conclusions: (a) Unlike the metabolic response to cold, the conscious sensation of cold is *not* inhibited by central warm-reception. (b) There is no central, conscious cold-reception in the range observed.

ception of cold at the skin is counteracted, like the metabolic response, by warm-reception in the central system. It seemed also important to know whether or not the peripheral reception of cold is supported and enhanced by central cold-reception.

1. *Conscious Sensation of Cold.*—Preliminary trials showed that it is somewhat difficult to define various stages of intensity in cold-sensation for evaluation. It is, however, readily possible to observe the subjective threshold of cold-sensation in a reproducible manner, when the stimulus is gradually applied to the entire body surface (except the head).

The subject, either untreated, precooled, or prewarmed for manipulation of his internal temperature, was immersed up to the neck in a waterbath at 37°C. By influx of cool water the vigorously stirred bath was cooled at a slow rate, approximately 1°C/hr. The subject was directed to report the first beginning of a cool sensation. The reported threshold values of bath or skin surface temperature were plotted against tympanic membrane temperatures, simultaneously recorded and shown in Figures 3 and 4, to find or to exclude a possible influence of internal thermoreception upon the sensation of cold.

*Result and discussion:* It appears from Figures 3 and 4 that, in the range observed, the influence of cranial internal temperature upon the threshold of conscious cold-reception was negligible. Only a slight decline toward higher internal temperatures is visible, more so in a lean individual (Fig. 3) than in an obese one

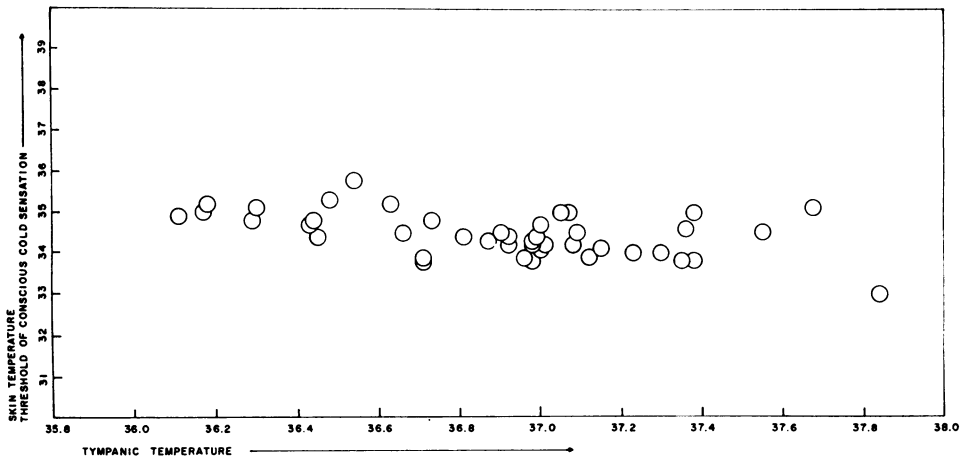


FIG. 4.—With an obese subject, thresholds of conscious cold-sensation were determined in baths of gradually decreasing temperature. Here the artefact of a temperature difference between surface and deep tissue is less noticeable. The independence of the sensation of cold from internal temperature is readily apparent.

(Fig. 4). This slight decline is an artefact. At the left side of the graph, skin and central temperatures were nearly identical. Here the actual receptor temperatures are presumably not different from the identical temperatures of the measured skin surface and the deep tissue below. On the other hand, at the right side of the graph an outward gradient in temperature existed between the higher internal and the lower surface temperature. Thermoreceptors located in this thermal gradient field must have had a temperature slightly above skin surface temperature. The surface measurements, which we had substituted for measurements at the receptors proper, must therefore have been too low in this region. We believe that consideration of this artefact and source of error permits us to say that there was no demonstrable influence of central temperature upon the sensation of cold in the range observed.

*Conclusions:* It is concluded that central cold-receptors with connections into the somesthetic cortex, responsive in the range observed, do not exist. It is also concluded that the afferent fibers from cutaneous cold-receptors for conscious cold-sensation bypass the posterior hypothalamic synapses in which the cold-impulses for metabolic action are so dramatically inhibited (see Figs. 2 and 6). If a central cold-reception would enhance the peripherally elicited conscious sensation of cold in man, or if this cold-sensation were inhibited by central warm-reception like the metabolic response, it is unthinkable that such enhancement or inhibition would not have resulted in a shift of the thresholds observed.

2. *Conscious Sensation of Warmth.*—To investigate the conscious sensation of warmth, a different way was developed from exploratory experiments. It was first attempted to elicit unpleasant warm-sensations by immersion in a bath too warm for comfort, in a moderately cool state of internal temperature. This proved to be impossible except for a sensation of burning pain, not warmth. It began as a transitory, overshooting response on entering a 39° or 40°C bath. Only at 42°C slight burning became a permanent sensation. Skin temperatures as high as these do not occur in air as a result of climatic conditions. Even at environmental

temperatures of 50°C skin temperatures seldom exceed 38°C. The thermally elicited burning sensation or pain, a useful warning signal against thermal burns, is therefore out of question as a driving force of behavioral temperature regulation in warm environments. The pleasant and agreeable sensation of warmth may be a driving force that tends to reduce cold stress, not heat stress.

The actual driving force of behavioral heat regulation against overwarming is best observed in baths of a lower temperature, 38.5°C. To an individual previously cooled for a normal or subnormal cranial internal temperature (36.5°C or lower), transfer into a 38.5°C bath appears pleasantly indifferent, not warm. This experience was unexpected. When skin thermoreception does not even recognize as warm a condition that would require an environmental temperature of more than 50°C in air, the skin cannot possibly be the origin of unpleasant, driving warm-impulses for behavioral temperature-regulation. Baths of a longer duration were therefore applied.

*Results:* On staying in a 38.5°C bath for 30 to 40 min the driving warm-sensation for behavioral control of body temperature appears in stages. It is felt with mounting intensity as internal cranial temperature, not skin temperature, increases. Although the transitions were gradual, four stages could be distinguished. They were considered attained as soon as the subject answered, one after another, the following questions:

- (1) Do you feel warm rather than cold or indifferent? (Stage 1)
- (2) Would you be more comfortable in cooler water? (Stage 2)
- (3) Let us know when you feel oppressed or restless. (Stage 3)
- (4) Let us know when you definitely want to leave the warm bath. (Stage 4)

Upon arrival at each one of these four stages the cranial internal temperature was recorded. It appears that a subject can reproduce the stages within  $\pm 0.3^\circ\text{C}$  of internal temperature at a constant skin temperature of 38.5°C (Fig. 5).

*Discussion:* The fact that all four stages, from indifference to thoroughly unpleasant heat, were subjectively experienced at the same skin temperature, 38.5°C, proves the existence of internal, conscious warm-reception. The only other alternative seems most unlikely, namely, that the mounting sensations of heat could have been a delayed response to cutaneous, not internal, reception. Thermoreceptors as a rule have overshooting rather than delayed response characteristics. Thermal inertia of such magnitude is out of the question for receptors under the skin surface. Compared with the precision of the autonomic responses of man the reproducibility of his internal warm-sensation in Figure 5 is not very impressive. However, in absolute terms of temperature, and for a sense not previously recognized to exist, it appears satisfactory.

It should be added that excitation of the cold-receptors of the skin quenched the internal perception of warmth effectively and swiftly in our tests. Even merely to remove the pleasant stimulus of warmth at 38.5°C from the skin by lowering bath temperature to 35.5°C (where cold-receptors do not yet respond) seemed to have an alleviating effect on the subjective warm-sensation. A supporting action of warm-impulses from the skin can therefore not be excluded; cold-receptor inhibition of the internally elicited sensation of heat seems to be certain. Such inhibition would readily explain the immediate relief derived from fanning the sweating skin in an overwarmed condition, or from cooling a hand in water.

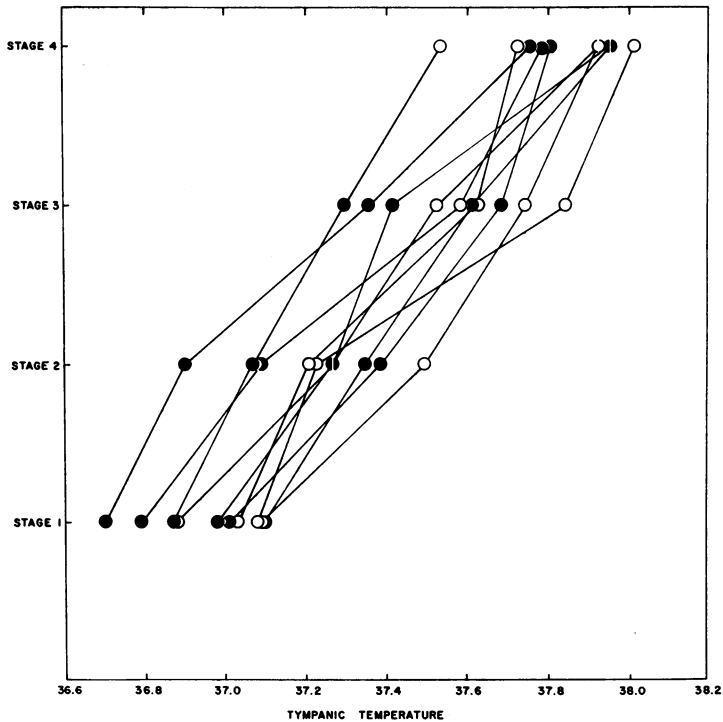


FIG. 5.—At uniform and constant skin temperature in a waterbath of  $38.5^{\circ}\text{C}$ , various stages of internal warm-sensation are experienced as internal cranial temperature increases. The stages range from pleasant indifference to almost unbearable heat.

The observation of internal warm-reception as the origin of heat-discomfort is consistent with results obtained by Winslow *et al.*<sup>7</sup> in 1937. While cold-discomfort was found by them to be closely correlated with skin temperature, warm-discomfort was closely correlated with their observations of sweating intensity. The link between their observations and the result of our tests is the quantitative relation between sweating and internal cranial temperature, recognized 22 years later.<sup>1</sup>

The experiments reported here do not permit one to locate anatomically the internal warm-sensor for conscious perception within the body core. Without evidence from animals this question would remain unanswered at this time. It is not likely that means will be found to stimulate a small circumscribed central area by heat on man in full consciousness. Fortunately, by inference from animals, one certain site comes under specific consideration. Together with a verbal presentation,<sup>8</sup> J. D. Hardy showed a motion picture which demonstrated impressively the "basking behavior" of a dog as a result of warming the preoptic region. This observation is consistent with our findings. As evidence of the anatomic location it may or may not be accepted. If not, the alternative would be to assume that a second internal warm-sensor exists and has yet to be found in man.

A summary of our findings on chemical, physical, and behavioral regulation of temperature is given with the postulated centers and pathways of Figure 6. Path-

ways of pain and pleasant warm-sensation have been omitted as irrelevant to the warm-discomfort for behavioral temperature regulation. Arrows pointing toward the cortex do not mean to exclude participation of lower levels in the subjective awareness of internal temperature. Yet, for intelligent behavior, synapses with cortical motor neurons are ultimately required.

3. *Summary.*—(i) The conscious sensation of cold in man is elicited by peripheral receptors. Unlike the response to cold by metabolic action, the conscious sensation of cold is *not* inhibited by central warm-reception, and central receptors for conscious sensation of cold seem not to exist in the range observed. (ii) At a uniform and constant skin temperature of 38.5°C various stages of warm-sensation may be experienced. These range from pleasant indifference to almost unbearable heat. The unpleasant sensation of the warm, driving force of behavioral temperature regulation in hot environment must therefore originate from a warm-sensor in a central, not peripheral, location, probably from the “temperature-eye” in the anterior hypothalamus.

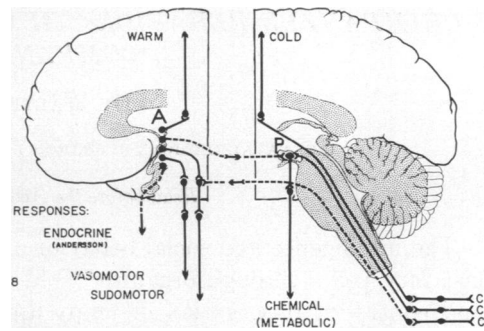


FIG. 6.—Together with the postulated components of autonomic temperature regulation the origins of heat- and cold-discomfort for behavioral temperature control are outlined. Common to both mechanisms is the predominance of central warm- and peripheral cold-reception. Like the retina, the internal warm-sensor elicits conscious sensations.

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<sup>1</sup> Benzinger, T. H., “On physical heat regulation and the sense of temperature in man,” these PROCEEDINGS, 45, 645 (1959).

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<sup>4</sup> Hemingway, A., T. Rasmussen, H. Wickoff, and A. T. Rasmussen, “Effects of heating hypothalamus of dogs by diathermy,” *J. Neurophysiol.*, 3, 329 (1940).

<sup>5</sup> Freeman, W. J., and D. D. Davis, “Effects on cats of conductive hypothalamic cooling,” *Am. J. Physiol.*, 197, 145 (1959).

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<sup>8</sup> Hardy, J. D., H. T. Hammel, and T. Nakayama, “Observations on the physiological thermostat in homoiotherms,” presented at the Ninety-Ninth Annual Meeting of the National Academy of Sciences (1962), and published as an abstract in *Science*, 136, 326 (1962).