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The Role of Skin Temperature in the Control of Sweating in Man

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by

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LIFE

Thomas V. McCaffrey, son of Mr. and Mrs. John D. McCaffrey, was born on November 29, 1948 in Chicago, Illinois. He received his early education in the Chicago area. In 1966 he entered Loyola University receiving the Bachelor of Science Degree in 1970.

In the summer of 1970 he began graduate studies at Loyola University in the Department of Physiology. The same year he entered the Loyola University Stritch School of Medicine. For the next four years he pursued a combined M.D., Ph.D. degree program, receiving the M.D. degree summa cum laude in 1974. He continued graduate work with Dr. Robert D. Wurster in the Department of Physiology as research associate until July 1975. In July 1975 he began residency training in Otorhinolaryngology at the the Mayo Graduate School of Medicine, Rochester, Minnesota. In 1980 he completed residency training and has been appointed to the Staff of the Mayo Clinic as Consultant in Otorhinolaryngology.

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I. INTRODUCTION

From a physical point of view, the regulation of deep body temperature consists of balancing those factors which produce heat loss with those factors which produce heat gain. Homeotherms by definition maintain a body temperature which is independent of environmental factors, indicating that some mechanism acts as a built in controller to maintain deep body temperature at a predetermined level. The quantification of body temperature is essential for such a system to act as a controller.

The two major sites of thermoreceptors in man are the hypothalamus (specifically the anterior hypothalamus-preoptic area) and the skin, although other thermoreceptors within deep body structures probably do exist.

The hypothalamic thermoreceptors are firmly established as essential in the regulation of heat loss mechanisms, including sweating, in man. But considerable controversy has existed over the importance of peripheral cutaneous thermoreceptors in initiating and sustaining sweating in hot environments. Benzinger (1) suggested that skin temperature had no effect on sweating as long as skin temperature was above 33°C. Although there was experimental evidence to support this concept (2), subsequent reports indicated that skin temperature was an independent input to the thermoregulatory center at temperatures above 33°C (3-9). More recently, Wyss et al (10) have produced experimental evidence that skin temperature has an insignificant effect on sweating rate in man.

This controversy has been perpetuated by the experimental difficulty of separately influencing central body temperature and skin temperature in a hot environment and the lack of agreement over an appropriate noninvasive measure of central (anterior hypothalamic) temperature, especially during thermal transients.

Although it is generally accepted that the temperature of the anterior hypothalamus-preoptic area (PO/AH) is the sensed central temperature for thermoregulation; this site is inaccessible in human experimental studies.

Rectal temperature was the first body temperature used to estimate the central temperature; however, it became apparent that rectal temperature responds slowly to central temperature changes. Benzinger utilized tympanic membrane temperature as a measure of central temperature, since he reasoned it measured cranial blood temperature and presumably hypothalamic temperature (11). Subsequently, other measurements of deep body temperature have been utilized, including esophageal (12) and right atrial blood temperatures (10). In each case it is argued that the measured temperature is a suitable indicator of hypothalamic temperature.

The purpose of the present series of investigations was to reexamine the role of skin temperature in the control of human thermoregulatory sweating in hot environments, and in addition, to attempt to reassess the validity of various measurements of central temperature, specifically tympanic membrane temperatures.

II. LITERATURE REVIEW

A. Central Thermoreceptors

The first clear demonstration of the thermosensitivity of the brain was made at the beginning of this century. In 1904 Kahn (13) heated the blood entering the brain from the carotid arteries and observed vasomotor and respiratory responses. Moorhouse (14) and later Hammouda (15) repeated these studies and obtained similar results. These workers suggested that the thermoregulatory centers of the brain are sensitive to the temperature of the blood reaching them.

In 1912 Barbour (16) attempted to localize the thermosensitive region within the brain by locally heating the brain with water passed through a closed tube. If strong heating or cooling was applied to the corpus striatum of rabbits, it produced changes in body temperature; warming lowered body temperature and cooling raised it. This observation was confirmed in cats by Prince and Hahn (17).

Cloetta and Waser (18) and Sachs and Green (19) challenged Barbour's results since they observed no thermoregulatory effects when they warmed the corpus striatum of the cat and rabbit.

The thermosensitive region of the brain was precisely localized by Hasama (20) as the hypothalamus. He produced profuse sweating of the footpads of cats when he warmed the base of the hypothalamus and the preoptic region.

Hammouda (15) found that if the third ventricle of the dog is perfused with warm saline, the dog will pant. The heating of the hypothalamus by the perfusion fluid was suggested as the reason for the thermoregulatory response.

These early studies had localized the thermosensitive region of the brain to the hypothalamus; but because the methods utilized produced warming of structures possibly distant from the site of stimulus, a precise localization was not possible.

With the introduction of sterotaxic techniques and localized heating using diathermy, it was possible for Magoun et al (21) to define the sensitive region as the ventromedial telencephalon. These authors pointed out that although this region is sensitive to temperature, the neuron pools which coordinated the heat loss mechanisms could be located at some distance from this region. These observations have been repeatedly confirmed by other authors in various species (22,23,24).

The first investigation of cold sensitivity in the hypothalamus was by Ström (25). By cooling the hypothalamus Ström was able to elicit vasoconstriction in the skin blood vessels, although he did not observe shivering. Kundt et al (26) and Hensel and Krüger (27) found vasoconstriction in ear vessels and shivering as well as a rise in rectal temperature of cats when the hypothalamus was cooled about 1°C. Placement of the thermode outside the hypothalamus failed to produce these effects.

Freeman and Davis (28) using heating and cooling found that thermoreceptor responses could be obtained from the anterior hypothalamus, but not the posterior hypothalamus.

By 1960 it was evident that central thermosensitivity was located within the hypothalamus. Heat loss or heat gain mechanisms could be elicited by cooling or heating localized regions of the brain in the region of the preoptic areas and anterior hypothalamus (PO/AH). From

these data several conclusions could be drawn: 1) There is a specific region of the brain which responds to temperature changes. 2) The region is in the anterior hypothalamus or preoptic area. However, the presence of actual thermoreceptors within the brain could only be inferred from these data.

In 1961 Nakayama (29) recorded for the first time neural activity related to changes in temperature of the PO/AH region. He found that approximately 20 percent of the cells in the PO/AH responded to local heating with an increase in frequency. However, none increased in activity in response to cooling. Later, Stuart et al (30) found some cells in the PO/AH which responded to cooling with an increase in frequency. Eiseman (31) and Eiseman and Jackson (32) measured the Q_{10} of PO/AH neurons in cats. The range of Q_{10}'s was from 1 to 8.5. Cells with Q_{10}'s greater than 2 (the expected Q_{10} based only on the dependence of metabolic activity on temperature) were designated warm receptors; those with Q_{10}'s less than 1 were designated cold receptors.

B. Peripheral Thermoreceptors

1. Cutaneous thermoreceptors

In 1844 Müller (33) proposed the concept of "specific nerve energies" by which he meant that the specificity of sensation resided within the nervous system and not in the stimulating agent. Volkman (34) extended this concept. He suggested that there were specific nerve endings responsive to each of the stimulus modalities.

Blix (35) found that hot and cold sensitivities were localized in specific areas which could be defined using pointed warm and cold metal probes. Blix mapped the location of these cold spots and warm

spots. Von Frey (36) related Müller and Volkman's concept of specific nerve energies to the observation of punctate sensitivity described by Blix. Von Frey suggested that the sensitivity of a cold spot was defined by the specific cold receptor in the defined region, while the sensitivity of a warm spot was defined by the specific warm receptor in the defined region.

Anatomical discoveries of end organs in the skin by Krause (37) and Ruffini (38) suggested that the end organs conferred specificity to the receptive modality of the nerve terminal. Controversy over the nature of end organs and their role in sensory specificity helped to expand the study of sensory processes. While Engelman (39) proposed that end organs were merely artifacts due to faulty technique, Von Frey (36) proposed that end organs conferred sensory specificity. Von Frey suggested that Krause end capsules were the sensory structures under each cold spot.

In 1955 Weddell and co-workers (40) concluded that encapsulated nerve endings were not essential for thermal sensitivity, since temperature sensitivity was present in the regions where encapsulated nerve endings were not present, for example the cornea (41).

Sinclair (42) went even further to state that sensory modalities were determined only by the pattern of neural impulses reaching the CNS. In other words, there are no specific fibers and no specific endings.

With the advent of single fiber recordings of sensory nerves, objective measures of the input to the CNS could be made. These

measurements resolved the issue of the type of information processing at the periphery.

Zotterman (43) and Hensel and Zotterman (44,45) studied the impulses from the lingual nerve of the cat during temperature stimulation of the tongue surfaces. Accurate thermal stimuli were applied by means of a thermode which would maintain a constant temperature and pressure on the tongue surface. They were able to define two types of temperature receptors by the pattern of discharge during maintained temperature and temperature changes.

In neurophysiological terms cutaneous thermoreceptors were found: 1) to have a static discharge at constant temperature, 2) to have a dynamic response to temperature changes with either a positive temperature coefficient (warm receptors) or a negative coefficient (cold receptors), and 3) not to be excited by mechanical stimuli within reasonable limits of intensity.

By the criteria of their dynamic response, cutaneous thermoreceptors are divided into the classes of warm and cold receptors. Irrespective of the initial temperature, a warm receptor will always show an overshoot of its discharge on sudden warming and an inhibition on cooling. A cold receptor behaves in the opposite way. In addition to their difference in dynamic behavior, the static frequency response curves of cutaneous thermoreceptors are different. Cold receptors have a maximum static discharge at approximately 25°C in the cat tongue while warm receptors have a maximum discharge rate at 38°C to 43°C (46).

Cold fibers are both myelinated and nonmyelinated while identified warm fibers have been only found to be nonmyelinated. Cold sensitive regions have been found to be more numerous than warm sensitive regions.

Several workers have suggested that the adequate stimulus for cutaneous thermoreceptor stimulation was the spatial temperature gradient [Dodt and Zotterman (47), Bazett and McGlone (48), Ebbecke (49), Rein (50), Windisch (51) and Oppel and Hardy (52)]. This concept was formulated as the thermocouple theory by Lele (53), Tyrrell (54), and Williams (55). Stimulation of the thermal receptors was believed to require a spatial thermal gradient between the superficial and deep regions of the skin. This theory was conclusively disproved by Hensel and Zotterman (56) and Hensel and Witt (57) who cooled the cat tongue with reverse gradient and demonstrated identical responses for cold receptors.

A more recent model of thermoreceptor behavior was proposed by Zerbst (58) based on the assumption of a chemical transmitter release coupled with diffusion of transmitter to an excitable membrane. Temperature alters the velocity coefficient of the chemical reaction and diffusion to different degrees.

The conclusions which can be reached on the basis of the present knowledge concerning thermoreceptors are: 1) thermoreceptors have a physiologic, but not necessarily anatomic specificity, 2) there is evidence of temporal coding in the transmission of temperature information to the CNS, 3) two types of temperature receptors based on dynamic sensitivity can be defined, cold receptors and warm receptors,

4) the adequate stimulus for a thermoreceptor is temperature and temperature change, but not spatial temperature gradient.

2. Deep body thermoreceptors

There is increasing evidence that there are thermoreceptors located in sites other than the skin and hypothalamus.

Simon et al (59) first demonstrated that cooling of the spinal canal produced an increase in shivering thermogenesis and a reduction of cutaneous blood flow. Further investigations in dogs (60) confirmed that the lowering of spinal canal temperature evoked shivering in the absence of changes in other central or peripheral temperature changes. Rautenberg and Simon (61) further demonstrated that shivering which had been evoked by general body cooling was enhanced by spinal canal cooling and reduced or abolished by spinal canal warming.

The thermosensitive neurons are probably located along the whole length of the spinal cord; however, Carlisle and Ingram (62) have shown in the pig that the cervical part of the spinal canal was more sensitive to thermal stimulation than the lumbar and sacral regions.

Thermal stimulation of the spinal canal produces thermoregulatory responses because of the thermosensitivity of spinal cord neurons and not stimulation of dorsal root afferents. This was shown by Meurer et al (63) who demonstrated shivering in response to spinal canal cooling in the dog with chronic bilateral transection of dorsal roots.

There is accumulating evidence that there are extra central nervous system deep body thermoreceptors. Bligh (64) found that when cold saline was infused into the abdominal vena cava of sheep during heat exposure, respiratory frequency dropped. Since there was no

change in temperature in the blood reaching the brain, he suggested that temperature sensitive structures were present near the vena cava. Rawson and Quick (65-68) have shown that intra-abdominal heating in sheep causes an increase in respiratory frequency in neutral and warm environments. Evaporative heat loss in these cases produced a fall in hypothalamic temperatures. They interpreted these data as evidence of deep body thermoreceptors possibly in the sheep rumen or great veins of the abdomen. Unilateral splanchnotomy resulted in the abolition of the response and suggested that the location of the thermoreceptors is in the walls of the rumen or intestine. This supports the contention that stimulation of spinal cord thermoreceptors is not a factor during intra-abdominal temperature stimulation (69,70).

Riedel et al (71) have compared the thermoregulatory response to spinal cord and intra-abdominal thermal stimulation. Spinal cord sensitivity was approximately four times that of intra-abdominal thermoreceptors; and while the spinal cord is sensitive to heating and cooling, the intra-abdominal receptors are only warm sensitive.

C. Central Integration of Peripheral Thermoreceptor Input

The thermoreceptor fibers enter the spinal cord with pain afferents via the dorsal root. A lateral bundle of fine fibers enters the zone of Lissauer while larger fibers enter medially and pass into the main portion of the posterior funiculus lying medial to the dorsal horn. Each root fiber bifurcates into a longer ascending and a shorter descending arm as soon as it enters the spinal cord. Most primary afferent fibers penetrate through the three dorsal laminae of the gray matter and enter lamina IV or lamina V. A few fibers terminate in the

substantia gelatinosa and arborize in the superficial layers (laminae I-III) of the dorsal horn, thus forming a complex intersegmental circuit.

Cells in the dorsal horn contribute axons which cross to the contralateral side via the anterior commissure and give rise to the lateral spinothalamic tract. The fibers of the lateral spinothalamic tract form an anteromedial segmental arrangement. The most lateral and posterior fibers represent the lowest portion of the body, whereas the more medial and anterior fibers represent the upper part of the body. There is also a sensory lamination with thermal sense fibers posterior and pain fibers more anterior. As the tract extends into the brain stem numerous collaterals are sent to the reticular formation and tegmentum. The tract terminates in the posterolateral ventral nucleus of the thalamus.

Some temperature sense information may ascend to the superior colliculus via the spinotectal tract.

Thermoreceptor fibers from the face have their cell bodies in the trigeminal ganglion. These fibers enter the pons and descend in the spinal tract of the trigeminal nerve with pain fibers. They synapse in the spinal nucleus of the trigeminal nerve. Within the spinal trigeminal tract there is a definite topographical grouping of fibers; fibers from the ophthalmic division are most anterior, fibers from the maxillary division are intermediate, and fibers from the mandibular division are posterior.

Axons from the spinal trigeminal nucleus pass ventromedially in the reticular formation, cross the median raphe, enter the contralateral

medial lemniscus forming the ventral trigeminal tract, and ascend to the ventral posteromedial nucleus of the thalamus.

Additional thermal sensory afferent fibers travel in the sympathetic nerves. These fibers enter the dorsal root of the spinal cord and ascend through multisynaptic pathways within the spinal cord (72).

There is considerable evidence that peripheral thermoreceptor input influences thermoregulatory responses. However, Wit and Wang (73) presented the first evidence that thermal afferent activity affected hypothalamic neurons. They recorded single unit activity in the preoptic and anterior hypothalamic region which was related to peripheral thermoreceptor activity. These observations have been subsequently confirmed by Hellon (74,75).

Boulant and Bignell (76) recorded single unit activity in the PO/AH area. They determined local thermosensitivity of these units and their sensitivity to peripheral temperature. The thermal coefficient for most of the units (78%) was the same for local and peripheral temperature changes. In units responsive to both local and peripheral temperature, peripheral stimulation usually produced a decrease in local thermosensitivity suggesting a competition for neuronal excitation between local and peripheral facilitory inputs. These data would suggest that the PO/AH region is not only the central thermoreceptive region, but also the region of integration of central and peripheral thermoreceptor activity.

D. The Thermoregulatory Controller

Claude Bernard (77,78) offered some of the first models of biologic regulation. These were based on the ability of biologic systems to

maintain a constant "milieu intereur." However, it took some time for these concepts to be applied to temperature regulation in animals and man. Richet (79) and later Ott (80,81) discovered that puncturing the base of the brain in cats and dogs and rabbits resulted in the production of fever.

In 1904 (82) Ott proposed that animals subjected to heat or cold tend to regulate their body temperature about a fixed point, and that this regulation is based on the thermotaxic centers which he had identified in the base of the brain. In 1913 Meyer (83) extended Ott's concept to include two opposing but integrated centers; a thermogenic center and a thermolytic center.

In 1948 DuBois (84) produced a descriptive model of human thermoregulation demonstrating the integration of cutaneous thermoreceptors, hypothalamic thermoreceptors and the effector organs, sweat glands, cutaneous blood vessels, and muscles.

By 1952 Hensel (85) prepared a more detailed model incorporating both stimulation and inhibition with the integration of temperature signals from the periphery and the central chemoreceptors. The central regulation was divided into a heat conserving center producing vasomotor changes and chemical thermoregulation and a heat loss center producing sweating and panting. This model clearly divided the processes of temperature sensing and temperature integration.

In 1959 Benzinger proposed his model of thermoregulation. He proposed a central warm receptor and a peripheral cold receptor (86). Sweating and vasodilatation were controlled by the central warm receptor, and shivering was driven exclusively by cold sensors in the skin

via a synaptic temperature insensitive center "P" in the posterior hypothalamus. Inhibitory pathways passed from the central warm receptor to the "P" center and from the peripheral cold sensors to the central warm sensor. Benzinger's model implied that skin temperature could not effect sweating above 33°C.

Benzinger's proposals resulted in considerable controversy in thermoregulation research producing a rapid development of thermoregulatory models in subsequent years.

Although Burton (87) as early as 1934 had proposed a mathematical model of thermoregulation, it did not have much influence on further research in thermoregulation.

In 1961 Wissler (88) prepared a mathematical model of thermoregulation which explained many of the concepts which have been set forth by Burton earlier. Wissler (89) divided the body into six roughly cylindrical segments representing the head, trunk, and extremities, each composed of an inner core, muscle, fat, and skin layers producing a total of 24 compartments. Heat transfer occurred between compartments by conduction or convection via the circulation. This model could predict many of the observed experimental findings but represented only the passive aspects of the thermoregulatory system since a closed loop regulator was not included in the model.

Closed loop complete models of the thermoregulatory system rapidly proliferated. Smith and James (90) suggested a thermoregulatory system based on local skin temperature effector loops regulating sweating and cutaneous blood flow. The gain of these loops was controlled by the central hypothalamic controller.

In 1961 Crosbie et al (91) had proposed an alternative model with regulation achieved by summation of signals from the hypothalamus and peripheral receptors. This model of central summation was challenged in 1966 by Stolwijk and Hardy (92) who suggested central multiplication of the temperature signals from central and peripheral thermoreceptors.

Stolwijk (93) has since modified his 1966 model suggesting that regulation is achieved by a central signal (90% hypothalamic plus 10% skin) multipled by local temperature action on sweat glands and cutaneous blood vessels. Subsequent work in animals has also suggested that peripheral and central imputs interact in a multiplicative manner, i.e., peripheral thermoreceptor imput alters the sensitivity of the central thermal controller (68,94,95).

Each of the last four models suggested have included cutaneous signals in the control of sweating, and as such tend to refute the Benzinger model which proposed the insignificant effect of skin temperature on sweating in warm environments.

Recently, Wyss et al (10) have again suggested that sweating is not influenced by skin temperature. Their data suggest that the apparent influence of skin temperature on sweating observed by others is based on time lags in their estimates of core temperature, and that by measuring blood temperature during thermal transients it becomes apparent that skin temperature has no effect on sweating.

The multiplicity of models and the fundamental disagreement over the role of central and peripheral receptors in the thermoregulatory effects is an indication of the difficulty in testing these models. The basic difficulty arises from the inability to separate easily

changes in core temperature from changes in peripheral temperature in warm environments. In warm environments with extensive peripheral vasodilatation, changes in skin temperature rapidly influence core temperature. If there are unidentified time lags in central temperature measurement, the model predictions will not reflect observations.

E. Innervation of Sweat Glands

Sweating consists of the release of the glandular secretion of the sweat glands onto the surface of the skin. The evaporation of this aqueous fluid lowers body temperature by the latent heat of vaporization of the water in the secretion. In the absence of glandular secretion, a relatively small amount of water vapor (insensible perspiration) diffuses across the skin barrier.

There are two types of sweat glands that are anatomically distinct. One type opens directly onto the skin (atrichial), and the other type opens into the lumen of a hair follicle (epitrichial). The sweat glands of thermoregulatory importance in man are atrichial in type, as are the sweat glands of the footpad of the cat.

Langley described the autonomic innervation of sweat glands in 1891 (96). He described preganglionic fibers leaving the anterior root and terminating in the sympathetic ganglia. The postsynaptic fibers are distributed to the skin and innervate the sweat glands.

Ring and Randall (97) have traced the myelinated and unmyelinated fibers from the spinal nerves to the glands. These fibers ramified and passed along the tubules where they entered the basement membrane and terminated near myoepithelial cells and secretory cells. Randall

et al (98) supported Hillarp's (99) proposal that postganglionic fibers divide into smaller branches which innervate several sweat glands. Randall called the sympathetic fiber and its sweat glands a "sudomotor" unit as an analogy to the skeletal muscle motor unit.

Wang et al (100-103) have investigated the central control of sweating in the cat's footpads. Several regions of the brain, including the cerebellum, cerebral cortex, midbrain, pons, and medulla may influence sweating activity.

Roth and Johnson (104,105) have described sweating pathways distributed in the anterolateral column in man. Wang described pathways in the corticospinal tract of cats.

F. Control of Sweating

1. Role of central thermoreceptors

In 1949 Bazett proposed a theory to account for the stability of the body temperature of homeotherms (106). This was based on the different temperature activity characteristics of warm and cold sensitive hypothalamic neurons. Vendrick has interpreted Bazett's theory in terms of a set point (107). The set point is the steady state body temperature which the effector system maintains. The theory assumes that warm receptors are linked to heat loss mechanisms such as sweating and panting, and cold receptors are linked to heat gain mechanisms such as shivering and nonshivering thermogenesis. Any perturbation which tends to increase central temperature will stimulate central warm receptors producing increased activity of the heat loss mechanisms and a fall in body temperature. A fall in body temperature will stimulate cold receptors producing an increase in heat generating or conserving

mechanisms. The temperature activity relationship of the warm and cold receptors in this way determine the set point body temperature.

Although the Bazett theory accounts for the stability of body temperature, it implies that hypothalamic temperature alone determines the level of heat loss or heat gain. Hammel et al (108-110) have modified this basic set point theory to account for peripheral influences on the thermoregulator. They have introduced the concept of a variable set point. The error signal in this system is always related to the difference between hypothalmic temperature and set point temperature, but the set point may be modified under the influence of peripheral signals.

Wyndham and Atkins (111) constructed a scheme (Fig 1) in which there are: 1) two main pathways - one from central warm sensors to heat loss effectors and the other from central cold sensors to heat production effectors; 2) there are crossed inhibitor pathways between these two pathways and; 3) peripheral inputs converge onto the main effector pathways.

There has been little argument on the role of central thermoreceptors in the control of heat loss and heat gain systems. However, the manner in which peripheral inputs are integrated into these major control pathways has been more controversial. (See subsection 3, role of cutaneous thermoreceptors.)

2. Role of local skin temperature

Kuno (112) and later Randall (113) observed local sweating when skin temperature was raised to 43°C. Gurrey and Bunnel (114)

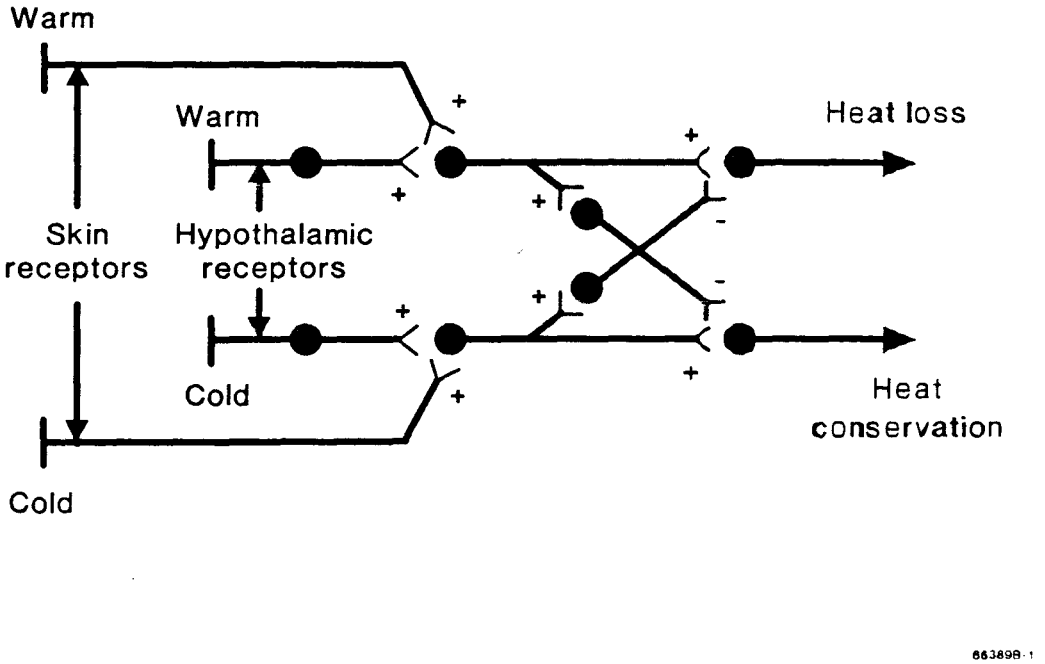

Figure 1. A diagrammatic representation of the relationship between hypothalamic and skin temperature sensors proposed by Wyndham and Atkins.

noted that this type of local sweating persisted even after sympathetic innervation of the sweat glands was interrupted. These observations suggested that sweat gland secretion could be stimulated by local temperature even in the absence of a neural secretomotor drive. Van Beaumont and Bullard (115) and MacIntyre, Banerffe and Bullard (116) induced sweating by local heating at moderate temperatures; however, the sweating responses which they produced required an intact innervation of sweat glands. They hypothesized that local temperature effected the nerve terminal sweat gland unit, but was not due to a thermal reflex. Nadel et al (5) have studied the effect of local skin temperature on sweating with a constant central sweating drive. They observed that local skin temperature had a multiplier effect on sweating rate. The Q_{10} of this effect was approximately 3. This suggested that transmitter release to the sweat gland was temperature dependent, and provides an explanation for the local temperature sensitivity of sweat glands.

3. Role of cutaneous thermoreceptors

The role of cutaneous thermoreceptors in the control of sweating has been an area of considerable controversy.

Beginning in 1959, (117,122) Benzinger et al published several papers on the control of human sweating derived from studies using the gradient layer calorimeter. At neutral and higher ambient temperatures the onset of sweating occurred at a very exact core temperature. Once initiated at this temperature, the sweating rate was proportional to the extent to which the tympanic membrane temperature exceeded the

threshold temperature. Changes in skin temperature had no effect upon sweating rate as long as skin temperature exceeded 33°C. From these results it was deduced that peripheral warm receptor input had no effect on sweating rate in man, and that at elevated temperatures only hypothalamic warm receptors were important in thermoregulatory sweating. However, at low ambient temperatures (those producing a skin temperature less than 33°C) which might be expected to stimulate peripheral cold receptors, sweating was initiated at higher tympanic membrane temperatures. These data suggested that peripheral cold receptors had an inhibitory influence on the efferent outflow from the warm receptors of the anterior hypothalamus to the sweat glands.

The conclusions by Benzinger that skin temperature had no effect on sweating at temperatures above 33°C was confirmed by Brebner and Kerslake (2). They showed that sweating was not affected by cooling the legs of human subjects when venous return from the legs was occluded by tourniquets. However, sweating was inhibited if the blood flow from the legs was not arrested. This supported the notion that central, but not peripheral thermoreceptors were effective in altering the sweating drive in man. The authors concluded from this work that they failed to demonstrate the existance of thermoreceptors in the skin of the legs which contributed to the control of sweat rate, but they did not assert the absence of such receptors.

The same year Brebner and Kerslake (3) produced evidence that peripheral thermoreceptors did influence sweating rate. By cyclicly heating the anterior chest wall, they found that sweating followed the heating of the chest with a delay less than two seconds; a period too

short to be due to changes in deep body temperature. However, as peripheral influence could only be demonstrated after sweating had become established, the initiation of sweating apparently depended upon core temperature first achieving a threshold value.

Belding and Hertig (123) found good correlation between sweating rates and tympanic membrane temperature and between sweating rates and skin temperature, but with abrupt changes in environmental temperature the changes in sweating rate more closely followed skin temperature than tympanic membrane temperature. They concluded that the control of sweating must involve input from peripheral thermoreceptors as well as hypothalamic temperature.

Wyndham (9) has confirmed the effect of skin temperature on sweating rate. He found that if sweat rate was plotted against rectal temperature at high skin temperature the curve was shifted to the left, and at low skin temperatures the curve was shifted to the right.

Wurster, McCook and Randall (4,8) measured sweating, cutaneous temperature, tympanic membrane temperature, and oral temperature during abrupt changes in environmental temperature. They noted inhibition of sweating during skin cooling while measures of core temperature were still rising.

Stolwijk and Hardy (124) subjected men to abrupt temperature changes while measuring rectal, tympanic membrane, and mean skin temperatures, metabolic rate, and weight loss. Sweating responded to the abrupt changes in ambient temperature before there were any apparent changes in core temperature. Total evaporative heat loss in these experiments could be correlated with the summation of thermal stimulation

of the skin and internal temperature sensors with a relative weight of 1 to 4.

The evidence presented indicates that the onset and subsequent rate of sweating is influenced to a great extent by core temperature, but that both core temperature at which sweating starts and subsequent rate of sweating are influenced by peripheral receptors.

This notion of the influence of peripheral receptors in sweating has again been challenged. Wyss et al (10) have presented evidence that skin temperature plays an insignificant role in the control of sweating in man. A water perfused suit was used to control skin temperature in four subjects, while skin, esophageal and right atrial blood temperature, sweating rate, heart rate, and forearm blood flow were measured. Multiple linear regression of sweating rate on right atrial blood temperature (a measure of core temperature) and skin temperature showed no significant effect of skin temperature on sweating rate. They argued that previous workers had shown an effect of skin temperature on sweating rate because of the time lag in their measures of core temperature. They demonstrated that if esophageal temperature instead of right atrial temperature were used in the regression analysis that their appeared to be an effect of skin temperature on sweating rate. They asserted that arterial blood temperature was the best measure of deep body and presumably hypothalamic temperature in man. Other measures such as tympanic membrane temperature, esophageal or rectal temperature have a definite lag with respect to blood temperature. Their final conclusions were in agreement with those of Benzinger that skin temperature above 33°C does not effect sweating rate.

The final consensus of the role of skin temperature on thermoregulatory sweating has, therefore, not been reached. The difficulty in separately influencing core and skin temperature at elevated ambient temperatures as well as the difficulty in interpreting various measures of deep body temperature appear to be responsible for this controversy.

G. Temperatures of the Body and Their Thermoregulatory Significance

1. Hypothalamic temperature

The studies cited in other parts of this review indicate that the hypothalamus is the overriding if not the only thermosensitive organ. It would appear, therefore, that measurement of hypothalamic temperature would be a useful determination in studying the thermoregulatory response of an organism.

Measurement of the hypothalamic temperature has been achieved in both anesthetized and awake unrestrained animals (125-132).

Abrams (129-131) has recorded hypothalamic temperature in unanesthetized cats at an ambient temperature of 22 to 25°C. Ingestion of cold fluid (5°C) caused a depression of hypothalamic temperature, while ingestion of water at body temperature was without effect. Otherwise hypothalamic temperature was quite stable when the animal was awake and active, but there were oscillations of up to 0.5°C when the animal was asleep.

There is evidence that the metabolic heat production of the brain is substantial and since the area of interface between brain and blood is greater than between brain and cranium, most of the heat of the brain is removed by circulating blood. McCook (132) noted a rise

in hypothalamic temperature in cats when the carotid arteries were occluded. Similarly, Hall (133) noted a rise in cerebral temperature in cats when the blood supply of the brain was occluded.

Although hypothalamic temperature is probably an important thermoregulatory temperature, its direct measurement is impossible in man under ordinary circumstances. In addition, other deep body temperatures may and do provide thermoregulatory input and reliance on a single deep body temperature is probably not valid.

Because of the need to obtain a measure of deep body temperature which could provide data on a hypothalamic as well as other possible thermoreceptor sites, various regions have been advocated for deep body temperature measurement.

2. Rectal temperature

Rectal temperature is widely used in experimental measurment of core temperature. The rectal temperature measurement is safe and easy although the sensor may become embedded in feces, and the response time may be prolonged. Rectal temperature is 0.2 to 0.5°C higher than the blood temperature leaving the left side of the heart due to heat production in the feces by bacterial action (134).

When there is an imbalance between heat production and heat loss and the body temperature is rising or falling, there is a delay of between five and ten minutes before a change in temperature of the blood leaving the heart is reflected in the temperature of the rectum.

Because of the long delay in rectal temperature it is unsatisfactory for dynamic studies during which there are nonsteady state conditions of heat loss or heat gain present.

3. Tympanic membrane temperature

Benzinger (117) considered tympanic membrane temperature a good indicator of the temperature of the blood supplying the hypothalamus, and therefore, hypothalamic thermoreceptor temperature. Since the blood supply of the tympanic membrane is derived in part from the internal carotid artery and the tympanic membrane itself has a low metabolic rate and thermal mass, temperatures recorded at the tympanic membrane should accurately reflect carotid artery blood temperature.

Although tympanic membrane temperature is superior to rectal temperature for measurement of deep body temperature especially during thermal transients when nonsteady state conditions are present, it is not without its own disadvantages. Although Benzinger (11) claimed that there was no discomfort in the placement of the tympanic membrane probe, this is not true in all cases. In addition, the surface skin temperature especially at low ambient skin temperatures may lower tympanic membrane temperatures [Benzinger and Taylor (11) and Marcus (135)] presumably because of cooling by venous blood draining the skin of the head and neck.

4. Esophageal temperature

In human studies esophageal temperature is a good index of the arterial blood temperature in the chest (136). Although there is some delay in recording rapid changes in aortic blood temperature at the esophagus due to the thermal inertia of the intervening tissues (10), during steady state esophageal temperature is a more reliable measure of aortic temperature than rectal temperature (137).

Since esophageal temperature will be influenced by anything ingested, it is not a suitable measure of deep body temperature under these situations. In spite of this restriction, esophageal temperature is the nearest approximation of central blood temperature which can be obtained short of catheterization of a major blood vessel or surgical implantation.

H. Interaction of Deep Body and Skin Temperatures

It has been assumed in much of the preceding discussion that core temperature and skin temperature measure two distinct compartments in the thermoregulatory system. However, the Wissler model of the thermoregulatory system clearly describes the interaction between these two compartments by conduction and convection (89).

Heat exchange between the periphery and the hypothalamus is primarily by convection since conductive heat losses are small through the cranium. In animals with a carotid rete Hayward and Baker (138-143) have demonstrated a countercurrent heat exchange between the carotid artery blood and the cavernous sinus blood.

In animals with a carotid rete blood reaching the brain from the carotid artery first traverses this plexus at the base of the brain. This plexus was first described by Herophilus and is present in the artiodactyls and in many carnivores. The carotid rete is an arterial plexus associated with the cavernous sinus and forms a countercurrent heat exchanger. In the rete, the arterial blood may be warmed or cooled by the cavernous sinus blood depending upon the relative temperatures of the arterial and venous blood.

Baker has shown that the carotid rete acts as a specific regulator of brain temperature. Cavernous sinus blood cooled by evaporative losses from the nasopharynx and nasal cavities reduces the temperature of the blood reaching the brain up to 2° below the carotid artery blood temperature. This protects the brain from thermal damage under periods of excessive heat load.

Such a mechanism makes the problem of defining core temperature more difficult. Since hypothalamic temperature has been generally considered the physiologically regulated deep body temperature, most indirect measures of deep body temperature rely upon blood temperature as an accurate indication of hypothalamic temperature. In those animal species with a carotid rete, blood temperature measurements may not accurately predict hypothalamic temperature, since it is effected by intracranial heat exchange.

The absence of a carotid rete in man rules out the efficient brain cooling mechanism present in the sheep and cat. But, it is possible that other brain temperature regulating mechanisms exist in man.

It is a common observation that head skin cooling contributes more to thermal comfort than other comparable sized areas of the body. This has been verified by several studies (144-147). This phenomenon may be attributed to several mechanisms: 1) head cutaneous thermoreceptors are more numerous and, therefore, have a greater input to the thermoreceptor areas of the brain; 2) head cutaneous thermoreceptors have a lower threshold than those of other body regions and, therefore, have a more pronounced effect on thermal regulation; and 3) cooling head skin effects the deep brain temperature by a countercurrent heat exchange mechanism.

III. METHODS

A. Climate Chamber

A double climate chamber was used to control ambient temperature (Fig 2). This climate chamber consisted of two independently temperature controlled rooms with a common wall. A passageway connected the two chambers. A copper screen bed on tracks could move between the two rooms with the head and foot ends of the bed sealing the passageway between the rooms when the bed was in position in one of the rooms. The time for moving the bed from one room to the other was less than three seconds.

In addition, an adjustable partition with a sealing diaphragm could be positioned around the subject at any location over the torso. This diaphragm was able to seal the passageway in a manner similar to the ends of the bed, permitting portions of the subject to be in each room simultaneously.

Room temperature was controlled with a proportional temperature control system permitting both heating and cooling over the range of 90°C to 15°C. Measured room temperature was within 1°C of control temperature at all times. Humidity was not controlled.

Room temperature was continuously monitored with thermistors, one thermistor for each control system, and a thermolinear device for a continous recording of room temperature. Instrumentation attached to the subject was mounted on the frame of the bed permitting continuous recording of sweating, skin temperature and deep body temperature while the subject was moved between rooms.

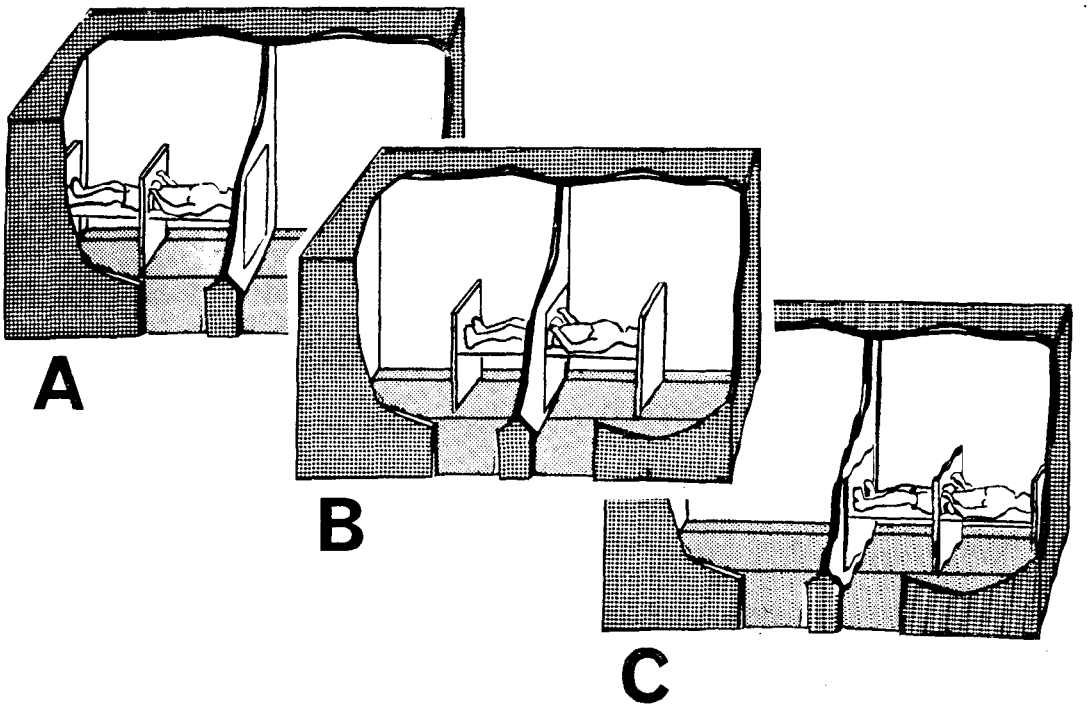

Figure 2. Cutaway view of the twin adjacent climate chambers. Two climate chambers have a common wall between them. Temperatures of the chambers are independently maintained by proportionately controlled heaters. The subject lies on a copper screen bed which can be moved quickly (2-3 sec) between the chambers. The head, foot, and diaphragm at the waist seal the connecting passage between chambers. In position A the subject is at the ambient temperature of the left chamber. In position B the subject's upper body is at the ambient temperature of the right chamber and lower body at the ambient temperature of the left chamber. At position C the subject is at the ambient temperature of the right chamber. Physiologic data from thermistors and resistance hygrometers measuring body temperature and regional sweating are carried by multiconductor cables through the ceiling of the chambers to recording equipment outside.

B. Temperature Measurement (Fig 3)

1. Tympanic membrane temperature

Tympanic membrane temperature was recorded in all experiments as an estimate of deep body (hypothalamic) temperature as described by Benzinger and Taylor (11).

A custom ear mold was fabricated for each subject out of silicone rubber (148). This mold had a central channel containing a polyethylene tube. With the ear mold in place a thermistor (YSI Model 520) was introduced down the polyethylene tube into the ear canal until contact with the tympanic membrane was made (this was noted by a scratching sound or sharp pain). The thermistor was then secured with a small jawed clamp (Fig 4). This technique permitted the positive contact of the thermistor against the tympanic membrane even during head movements. The short time constant of the thermistor probe (0.1 sec) permitted accurate recording of rapid changes in tympanic membrane temperature.

The thermistor probes were individually calibrated against a precision mercury thermometer, and their output was monitored by a stable bridge circuit balanced at 37°C.

2. Esophageal temperature

During some of the studies to be described, esophageal temperature was measured as an estimate of deep body temperature.

A thermistor (YSI Model 401) was introduced through the nose and passed into the esophagus with the help of some sips of water. The thermistor was advanced to the level of the left atrium and the lead secured to the nose with tape. This position of the thermistor probe

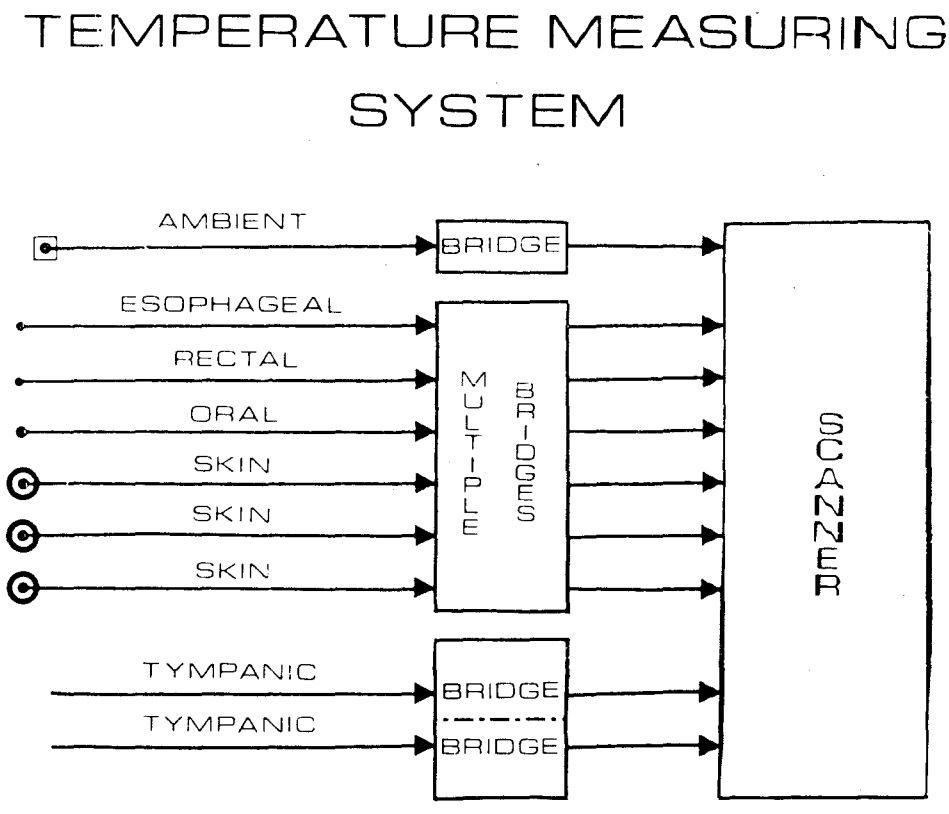

Figure 3. Temperature data from thermistors located in the climate chambers and on the subject were scanned at predetermined intervals and punched on paper type for later analysis.

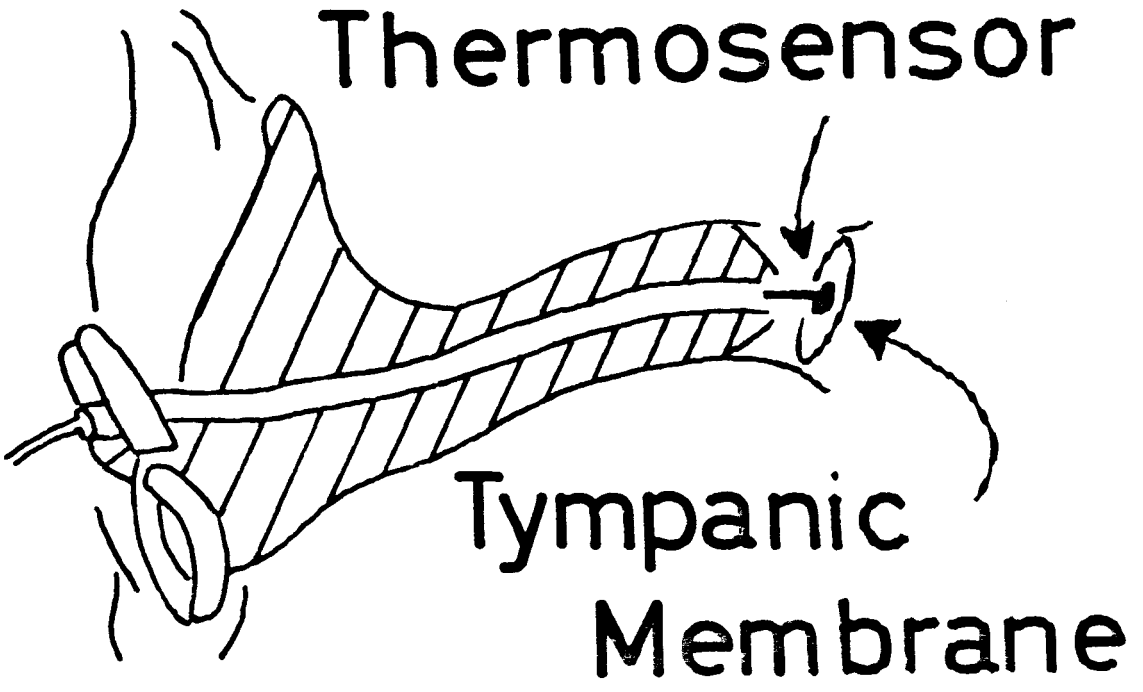

Figure 4. Tympanic membrane temperature was recorded by placing a thermistor (YSI Model 520) against the tympanic membrane. Contact was maintained by mounting the thermistor in a custom-made silicone rubber ear mold. This system permitted positive contact to be maintained without discomfort during head movements.

was confirmed by a chest roentgenogram. Subsequent placements were then based on the measured position as a distance from the nares.

3. Rectal temperature

Rectal temperature was measured in all studies. A thermistor (YSI Model 401) was introduced 10 cm beyond the anal sphincter and secured in place with tape.

4. Skin temperature

Skin temperature was measured at 12 locations. These locations were selected as representative regions of the body for the purpose of calculating mean skin temperature.

All skin probes were matched thermistors (YSI Model 426), mounted on lucite rings 3 cm in diameter, which permitted easy attachment of the probes to the skin surface (Fig 5). They also assured a constant pressure of the probe surfaced on the skin and prevented the probes from turning over.

Skin temperature was recorded from all 12 regions at 30-second intervals. These recordings were used to calculate mean skin temperature ($\bar{T}_S$), and when upper and lower bodies were individually heated or cooled, mean upper ($\bar{T}_{SU}$) and mean lower body ($\bar{T}_{SL}$) temperature was also calculated.

Weighting factors were derived from DuBois skin areas of each of the representative regions recorded (149). The weighting formulas are given below. The skin temperatures measured were forehead (T_{fh}), forearm (T_{fa}), arm (T_{ar}), palm (T_{pa}), upper chest (T_{uc}), lower chest (T_{lc}), upper abdomen (T_{ua}), lower abdomen (T_{la}), thigh (T_{th}), leg

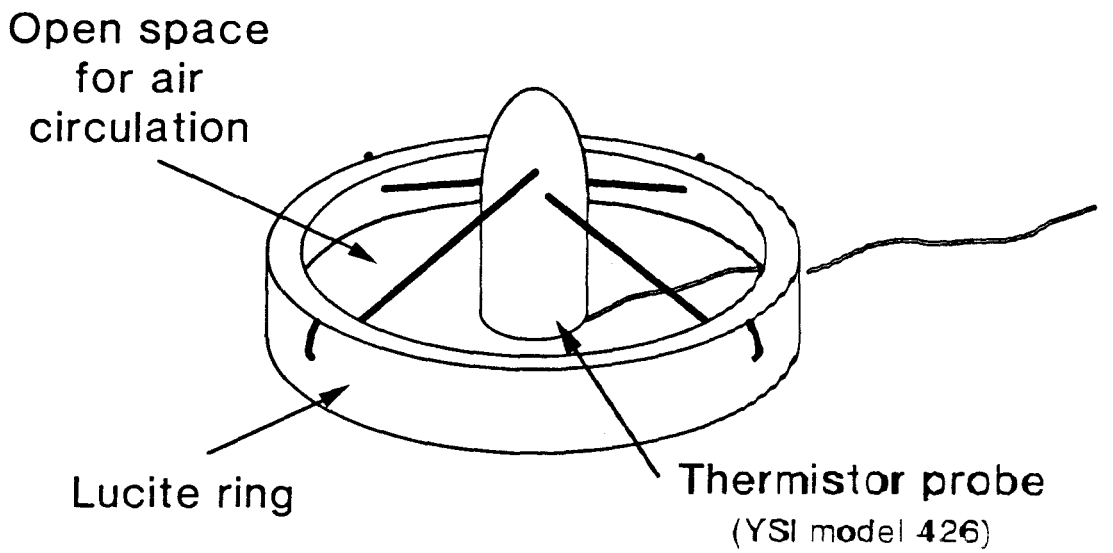

Figure 5. Skin thermistor probe (YSI Model 426). The thermistor probe was mounted on a lucite ring to maintain constant skin pressure and permit free air circulation around the thermistor and adjacent skin.

(T_{lg}), dorsum of foot (T_{do}), and plantar foot (T_{pl}). The weighting equations are:

$$\bar{T}_{SU} = .14\ T_{fh} + .14\ T_{ar} + .14\ T_{fa} + .10\ T_{pa} + .16\ T_{uc} + .16\ T_{lc} + .16\ T_{ua}$$

$$\bar{T}_{SL} = .22\ T_{la} + .32\ T_{th} + .32\ T_{lg} + .07\ T_{do} + .07\ T_{pl}$$

$$\bar{T}_{S} = .07\ T_{fh} + .07\ T_{ar} + .07\ T_{fa} + .05\ T_{pa} + .08\ T_{uc} + .08\ T_{lc} + .08\ T_{ua} + .11\ T_{la} + .16\ T_{th} + .16\ T_{lg} + .035\ T_{do} + .035\ T_{pl}$$

C. Sweating Measurement

1. Hygrometry

The basis of sweating measurement in these studies was resistance hygrometry. Evaporative water losses from measured regions of skin (beneath plastic capsules) was determined by multiplying absolute humidity of the air leaving the capsule by the flow rate of air drawn through the capsule. The air was dried, using a hydroscopic desiccator before it was drawn into the capsule so no correction needed to be made for the initial humidity of the air. This principle is described by the equation below where $\dot{Q}$ is the evaporative loss in mg/min, F is the flow rate of air in liters per minute, and H is the absolute humidity of the air leaving the capsule and HO the humidity of the air entering the capsule in mg/L. Since HO is very close to 0 it was not measured in this study.

$$\dot{Q} = F \times (H-HO)$$

Absolute humidity can be measured by several methods including wet and dry bulb thermometers, dew point, and the resistance of specific hydroscopic films. Of these methods only the last two, dew point measurement and resistance measurements of films, are useful in the

rapid, continuous determination of small variations in humidity needed for sweating measurement.

Dew point hygrometry is unsurpassed as an accurate measure of humidity over a wide range, and as such, was used as the calibration standard for the resistance hygrometers used in the study.

Resistance hygrometers (Panametrics) were used to measure the humidity of the air leaving the sweat collection capsules. These hygrometers were mounted in a brass constant temperature (41°C) manifold to prevent condensation and thermal drift. The output of the resistance hygrometers were recorded by the data collection system along with temperature measurements at 30-second intervals.

2. Sweat collection system

The sweat collection apparatus is diagramed in Figure 6. Sweating rate was determined by passing dry air at a measured flow rate (0.5 L/min) over the skin using plastic capsules covering an area of 9.8 cm^2. The air was then passed through resistance hygrometers (Panametrics) which had been calibrated against a precision dew point hygrometer (see below). The hygrometers were maintained at a constant temperature block to prevent thermal drift. The system had a measured time delay of five seconds due to the length of the connecting tubing.

Accurate measurement of sweat production required complete evaporation of the sweat from the skin surface. At a flow rate of 0.5 L/sec sweat evaporation was complete at all levels of sweating encountered in the present study. This was confirmed by the absence of liquid sweat under sweat capsules as well as the rapid decline in hygrometer output during body cooling (Fig 14-16). If liquid sweat was

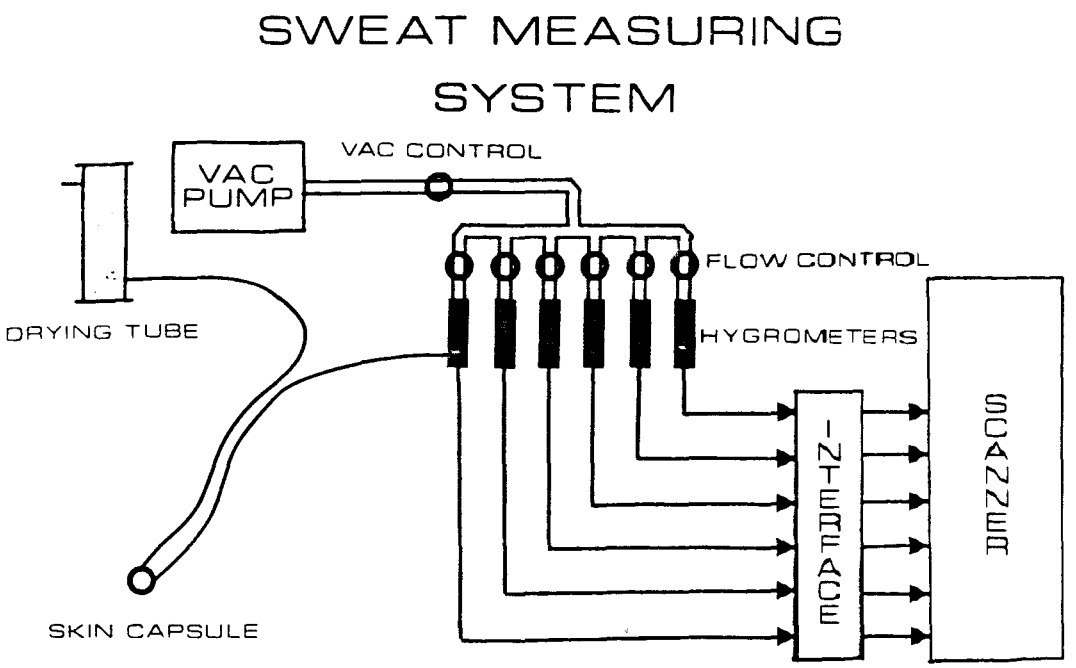

Figure 6. Diagrammatic representation of the sweat measuring technique. Dried room air was drawn over the skin covered by a capsule covering 9.8 cm^2. The air leaving the skin capsule passed through a resistance hygrometer. The output of each hygrometer was scanned at predetermined intervals and recorded on paper tape for later analysis. To prevent thermal drift, the hygrometers are maintained in a constant temperature block at 41°C. The system had a measured time delay of 5 sec due to the length of the connecting tubing.

present under the collection capsule, there would be a measurable delay in hygrometer output after sweat production was inhibited as a result of excess liquid sweat evaporated from the skin surface.

3. Calibration

The hygrometers were individually calibrated against a precision dew point hygrometer (Cambridge Systems Model 880). The calibration was done by placing the dew point hygrometer in circuit in series with the resistance hygrometer. Dry air was then passed through an evaporation chamber where a variable surface of distilled water was exposed by raising and lowering the level of water in a conical funnel. The water was maintained at a constant level until the dew point hygrometer and the resistance hygrometer maintained a steady reading (5 to 10 min). A series of measurements were made to calibrate the hygrometers over the desired range of absolute humidity (1 to 10 mg/L). These calibration curves for each hygrometer are shown (Fig 7). A complete calibration was repeated at one-week intervals, and an abbreviated calibration (2 points) was repeated before each study. All hygrometers maintained stable calibration constants throughout the study.

The output of the hygrometers were not linearly related to absolute humidity, but by logarithmic transformation the output could be linearized. These regression lines were used to convert hygrometer output to absolute humidity.

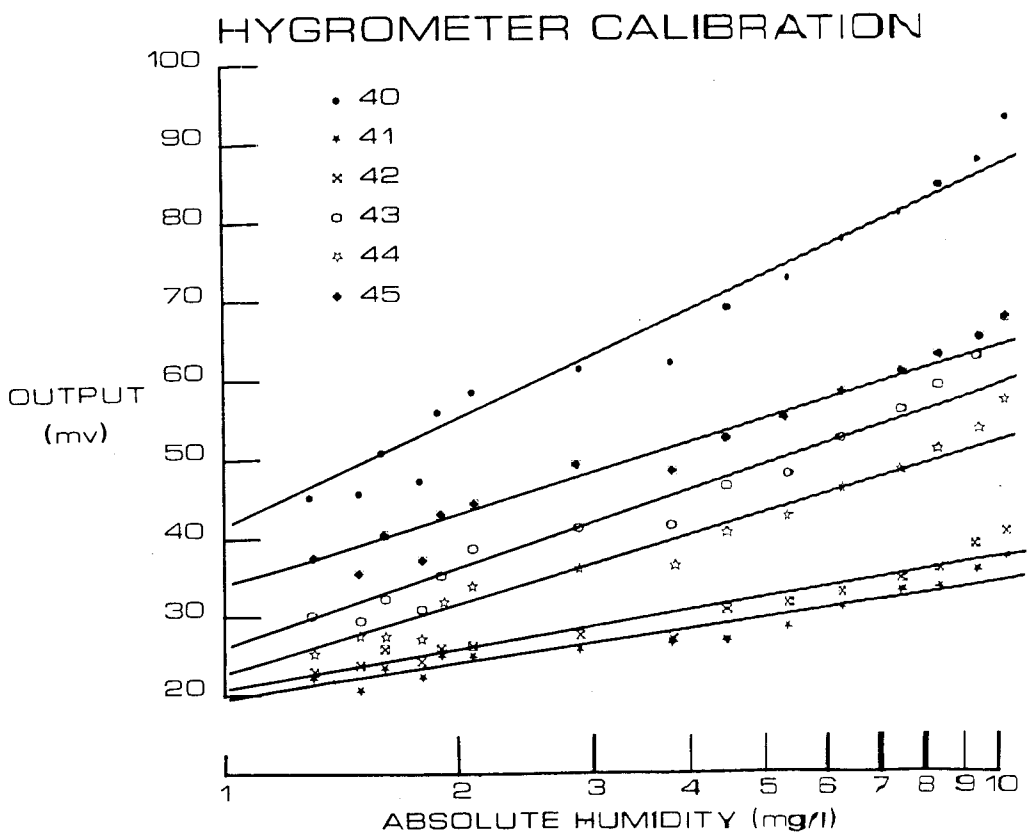

Figure 7. The calibration curves for the six hygrometers (channels 40-45). The straight lines represent logarithmic least squares fits for each transducer. From these curves, the sweating rate could be calculated from the hygrometer output.

D. Data Recording and Analysis

1. Data collection system

The data collection system (Fig 8) consisted of several subsections. The first was a series of identical bridge circuits incorporating one of the 400 series YSI thermistors. These probes were matched and interchangeable. As noted above, esophageal and rectal temperature were measured using the YSI 401 probe, and cutaneous temperatures were measured using YSI 426 probes. In addition, individual bridge circuits were calibrated for the YSI 520 probes used to measure tympanic membrane temperature. All temperature bridges were constructed to produce an output in millivolts equal to the temperature. These outputs had a precision of .01°C.

Because the wide range of ambient temperatures thermolinear devices were used to measure ambient temperature. The output of these devices in millivolts was equal to the temperature in °C.

Hygrometer output in millivolts was arbitrary, and individual calibration curves were constructed for the hygrometers, relating hygrometer output to absolute humidity.

The output of all temperature and hygrometer circuits were scanned at 30 second intervals by a scanning digital voltmeter controlled by the master clock. The output of each circuit was integrated for one second by the analog to digital converter. Each digital output was individually displayed and simultaneously punched in BCD (binary coded decimal) format on eight level paper tape by a paper tape punch (Tally).

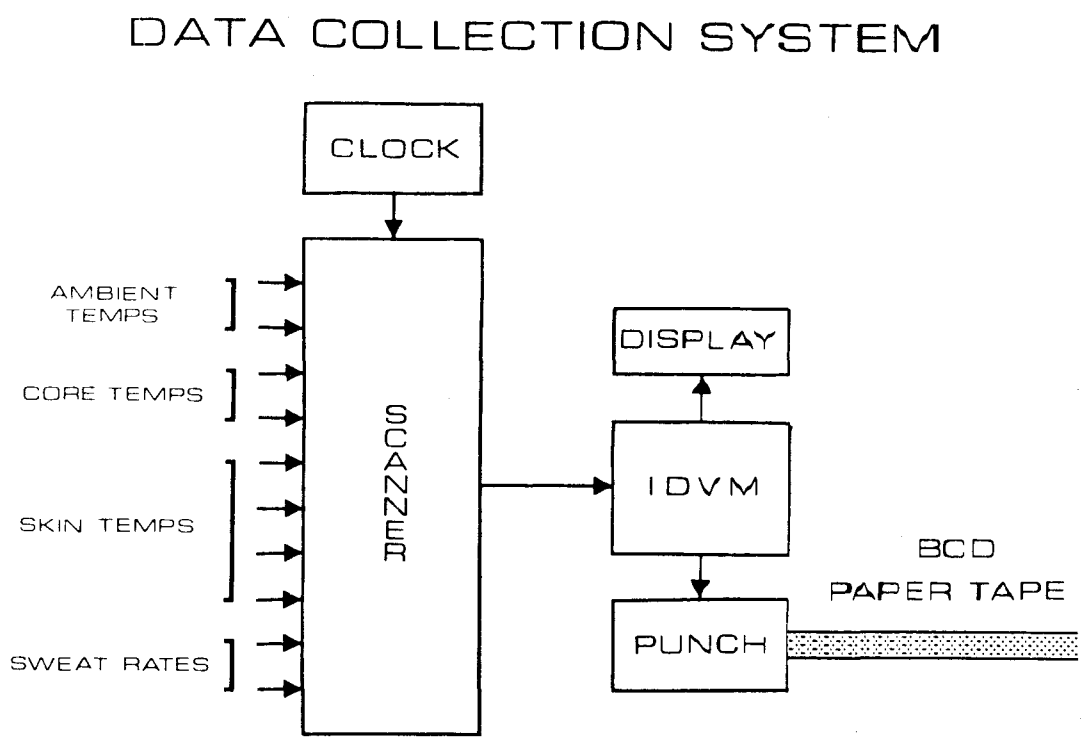

Figure 8. Block diagram of the data collection and recording system. Thermistor and hygrometer outputs were scanned at a predetermined clock rate. The data was digitized and punched in BCD format on paper tape. The paper tape was later read on a PDP-12 computer for final analysis.

Each segment of the data recorded consisted of the time, deep body temperatures, skin temperatures, ambient temperatures, and sweating rates (hygrometer outputs).

Sixty to 90 minutes (120 to 180 data segments) were recorded for a typical study.

2. Data analysis system

The data analysis was carried out on a PDP-12 computer (Digital Equipment Corporation) with associated memory, mass storage devices, and paper tape reader. The data analysis software system consisted a multisegment program written in Fortran IV and assembly language.

The data tape recorded during the study was read by the program and converted to floating point representation and stored on magnetic tape. These data were then available for plotting and further analysis.

Data analysis consisted of calculation of sweating rate from the hygrometer outputs and calibration data, calculation of mean weighted skin temperature, mena sweating rate, and regression analysis of the data. Statistical analysis techniques are described separately for each of the individual investigations.

VI. INVESTIGATIONS

A. Effect of Head Skin Temperature on Tympanic and Oral Temperature in Man (150)

Since the studies of Benzinger (1,11), the tympanic membrane temperature has been used extensively as an indicator of core temperature and perhaps of hypothalamic temperature in thermoregulatory studies in humans. However, a direct comparison of hypothalamic and tympanic membrane temperatures has not been made in humans. Such comparisons have been made in the cat by Randall et al (151), in the rabbit by Tanabe and Takaori (152), and in the monkey and cat by Baker et al (153). These studies indicate a good correspondence between hypothalamic and tympanic membrane temperature except during carotid occlusion.

1. Methods

The subject sat quietly from 0.5 to 1 hour before the beginning of the experiment in a room with ambient temperature of 22 to 28°C. Bilateral tympanic membrane temperatures were recorded by means of thermocouples (0.1 mm diameter) or thermistor probes (Yellow Springs Instrument, model 520) inserted in silicone rubber ear molds (148). These ear molds extended down the auditory meatus to within 2 to 3 mm of the tympanic membrane. The thermocouple or thermistor was passed down the tubing of the ear mold until positive contact was made with the tympanic membrane (sharp pain and/or scratching sound on the membrane) and was fixed in this position by a small clamp.

Similar thermocouples or thermistors were used to measure temperature on both right and left sides of the tongue. To minimize the

temperature influence of one side of the mouth upon the other, the thermocouples were placed far back under the tongue, lateral to the lingual artery and vein. Esophageal temperature was measured by means of a thermistor probe (Yellow Springs Instrument, model 401) that was passed through the nose down the esophagus, 35 to 40 cm beyond the nares. Roentgenolographic evaluation of the subject with esophageal thermistor in place showed that the thermistor was located at the level of the heart adjacent to the left atrium. This placement was felt to be optimal for the determination of central blood temperature (137). These temperatures were recorded by means of an oscillograph (Hartmann and Brown Co. or Grass Instrument Co.).

Cutaneous areas of the head and neck were simply heated and/or cooled by means of common rubber water bags filled with hot (45-50°C) or cold (3-4°C) water. These bags were held firmly to the skin surface by the subject. Care was taken to prevent thermal exchange between the rubber bag and the thermocouple leads or the skin around the mouth or pinna of the ear. The cutaneous areas of the head and neck that were heated or cooled are illustrated in Figure 9. Area 1 includes the lower forehead, upper nose, and upper cheek. Area 2 is the top, back region of the scalp. Area 3 is the side of the neck.

2. Results

To demonstrate the possibility of thermal exchange between head skin and the tympanic membrane, bilateral tympanic membrane temperatures were recorded simultaneously while one side of the face (area 1) was heated and the corresponding opposite side of the face was cooled (Fig 10).

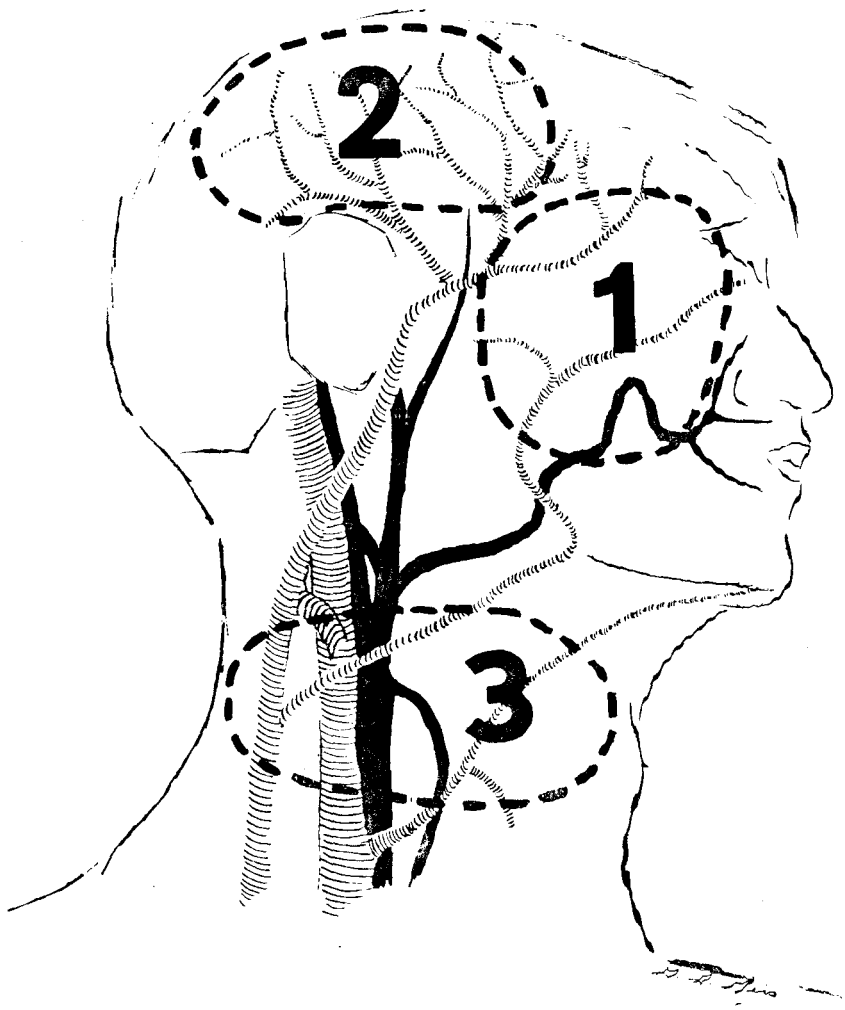

Figure 9. Diagram of the close relationship between the veins (striped) draining of the highly vascular face and scalp and the arteries (solid) supplying the head and intracranial structures. The regions used for local heating and cooling are labeled 1, 2, and 3.

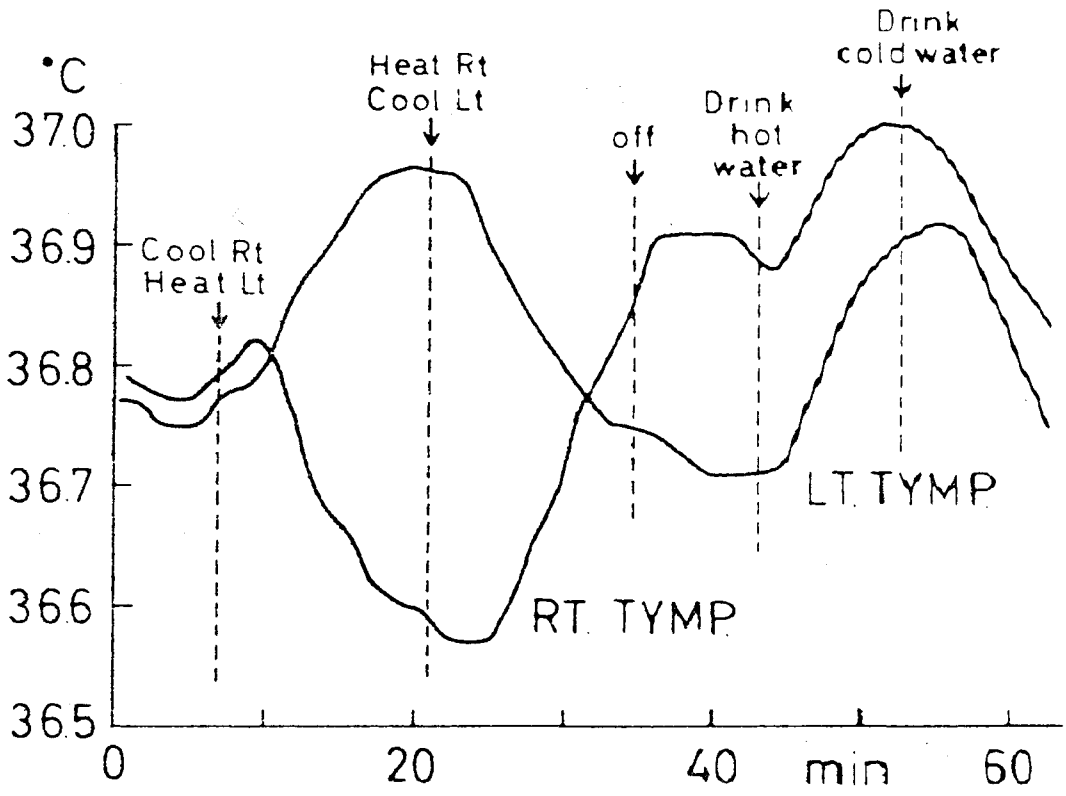

Figure 10. Right and left tympanic membrane temperatures during localized heating and cooling of area 1 of the head and after drinking hot and cold water.

After both tympanic membrane temperatures stabilized the right side of the face was cooled while the left side was heated. The right tympanic membrane temperature decreased sharply, and the left tympanic membrane temperature increased two to three minutes after the application of the rubber bags. After approximately 14 to 15 minutes, the opposite was performed (i.e., the right side was cooled and the left side was heated). The maximum difference obtained between the right and left tympanic membrane temperatures was 0.4°C. Two minutes later, the left tympanic membrane temperature began to decrease while the right increased. At minute 34 both rubber bags were removed; and consequently, both tympanic membrane temperatures leveled off. The subject drank approximately 0.5 liters each of first hot water (46°C) and then cold water (3°C) 9 to 10 minutes later. Although the left and right tympanic membrane temperatures were vastly different beforehand, both temperatures showed similar changes from the ingestion of hot and then cold water.

To determine if these responses involved other cutaneous regions of the head, the side of the face (area 1), the top of the head (area 2), and the neck (area 3) were separately heated while the contralateral areas were cooled (Fig 11). Oral and tympanic membrane temperatures were measured on the same side of the head (right). Both the oral and tympanic membrane temperatures followed the changes in cutaneous temperature on the same side of the head. The responses of oral temperature were less consistent and less extensive than those of the tympanic membrane temperature.

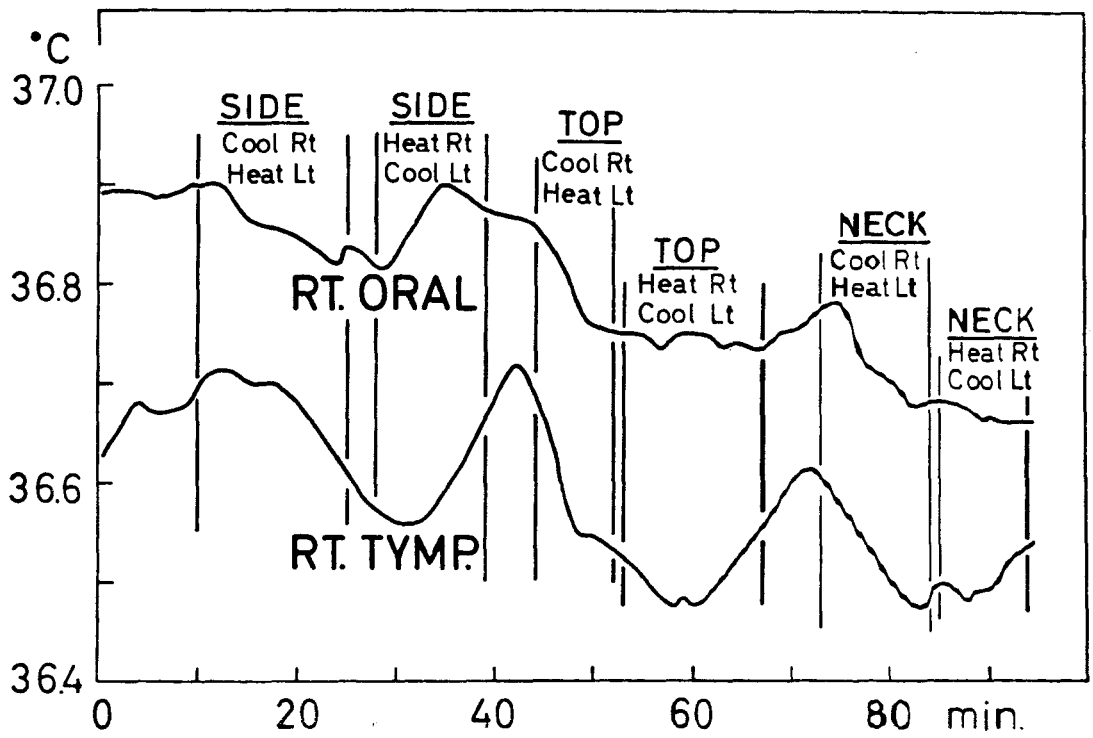

Figure 11. Right oral and tympanic membrane temperatures during heating of side (area 1) and top (area 2) of the head and neck (area 3).

In Figure 12 the bilateral tympanic membrane temperature responses are shown to heating and cooling the side of the face (area 1) while esophageal temperature is measured. If the tympanic membrane temperature changes were due to changes in blood temperature at the aortic arch the esophageal temperature changes would correspond to tympanic membrane temperature changes. The esophageal temperature was about 0.2°C below the tympanic membrane temperatures before the experimental procedures were initiated and remained relatively constant until minute 25. Then esophageal temperature showed a transient decrease when the left tympanic membrane temperature was falling rapidly and the right tympanic membrane temperature was slowly rising but was still some 0.2°C below the control temperature. It is concluded that the changes in tympanic membrane temperatures are not due to changes in the temperature of the ascending blood. Again a temperature gradient of over 0.4°C existed between left and right tympanic membrane temperatures.

In Figure 13 body temperature changes were made that did not involve the alteration in head skin temperatures directly in order to compare the relative changes and time course of tympanic membrane and oral and esophageal temperature.

During a suitable control period tympanic membrane, oral, and esophageal temperatures were stable at 37.30, 37.15, and 36.95°C, respectively. At minute 7 both feet were placed in a water bath at 42°C. Shortly thereafter, the esophageal temperature started to fall. This change was followed in sequence by the tympanic membrane temperature and later the oral temperature. The fall in temperatures ranged from

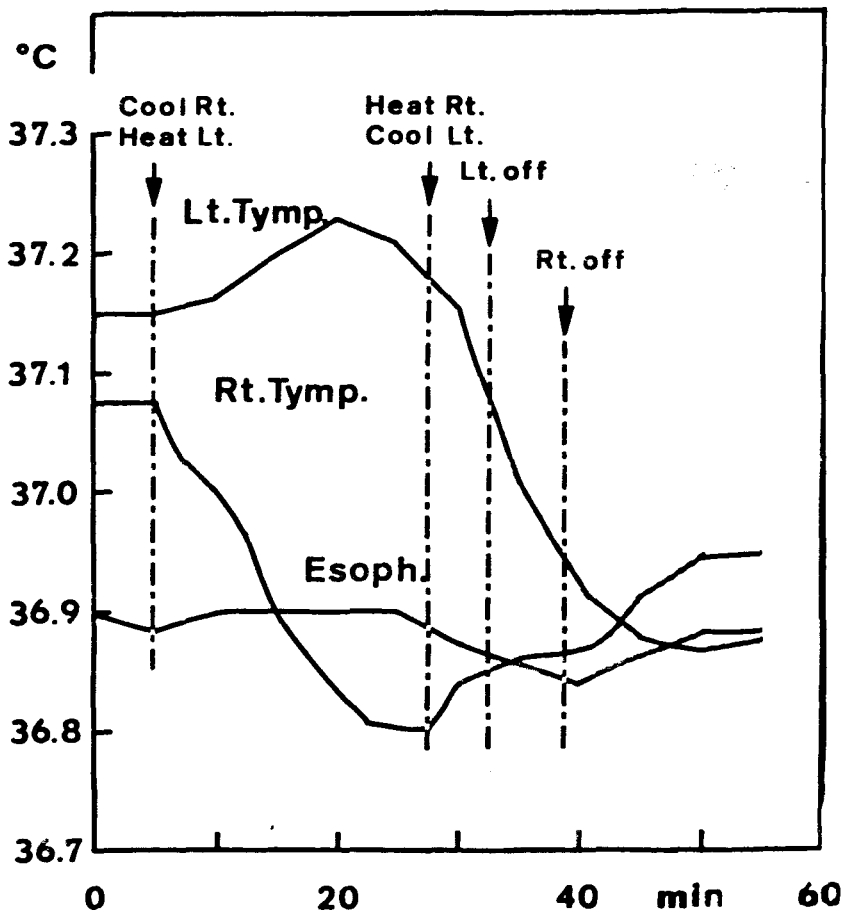

Figure 12. Right and left tympanic membrane and esophageal temperature during heating and cooling of area 1 of the head.

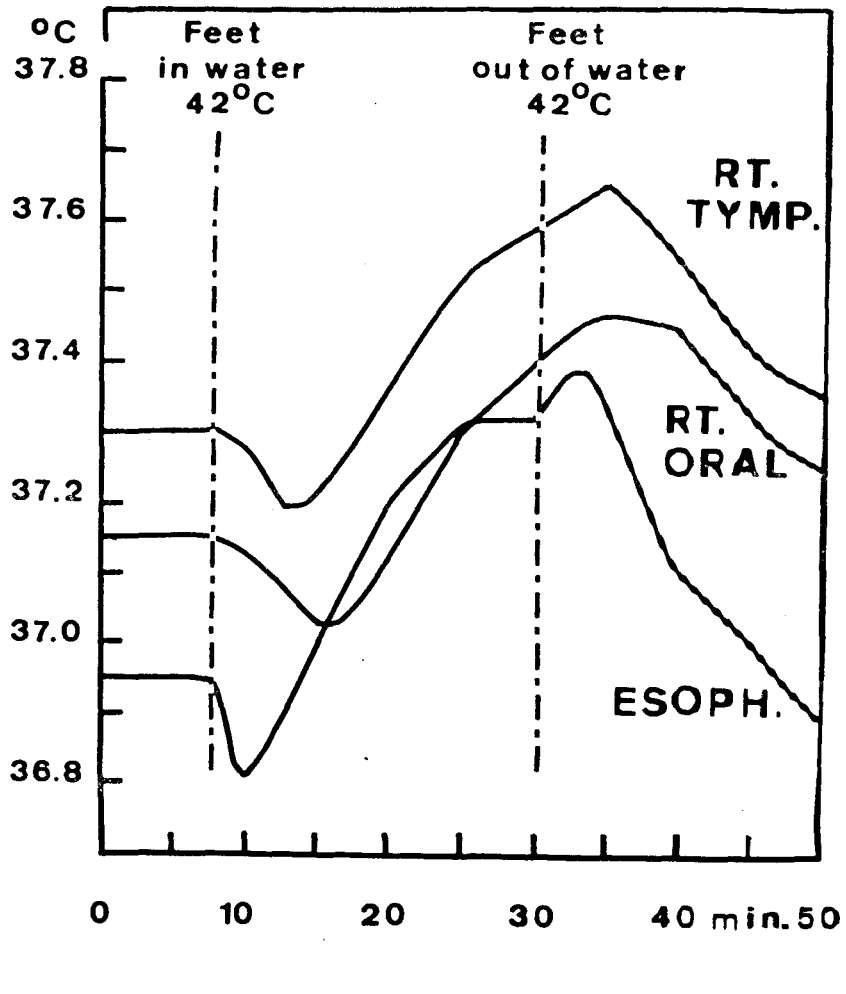

Figure 13. Right oral and tympanic membrane and esophageal temperature while heating feet and legs in 42°C water and recovery.

0.10 to 0.15°C, being greatest for the esophagus. Then sequentially, esophageal, tympanic membrane, and oral temperatures increased steadily. Shortly before removing the feet from the water bath, esophageal, tympanic membrane, and oral temperatures had risen 0.36, 0.30, and 0.27°C, respectively, from control levels. When the feet were removed, esophageal temperature began to rise again for two minutes, while tympanic membrane and oral temperatures continued to rise for the next three to four minutes. Then esophageal temperature decreased rapidly followed by tympanic membrane and oral temperatures.

3. Discussion

Benzinger (11) attempted to find a convenient location in man to measure temperatures that were similar to the hypothalamic temperature and suggested the tympanic membrane. To support the validity of this location, he measured on one subject temperatures of structures in the cranium which were near the hypothalamus or internal carotid artery or which, he held, were supplied by the internal carotid artery. During simultaneous recordings of these temperatures, as well as that of the tympanic membrane, the subject was given ice. This resulted in similar temperature alteration on all recorded cranial areas.

Anatomic studies reveal that the tympanic membrane is supplied by two to three branches of the external and one branch of the internal carotid artery. Furthermore, the blood supply to the nasopharynx and paranasal sinuses used in Benzinger's comparison is also by way of both external and internal carotid arteries (154). Correlation of hypothalamic temperatures with tympanic membrane temperature is further

complicated by differences and variations in local metabolism and blood flow of these structures.

Oral temperature has also been used in human thermoregulatory studies as a correlate of core temperature. The oral cavity is almost entirely supplied by branches of the external carotid artery. No comparisons, however, have been made between oral temperature and tympanic membrane or other cranial temperatures.

Esophageal temperature has become a common estimate of core temperature because of its proximity to the heart and great vessels (155). It is also noted that esophageal temperature usually follows thermal transients more rapidly than tympanic temperature (155).

When localized regions of the skin of the head were heated or cooled, the tympanic membrane temperature changes were observed. These results confirm the observation that head heating has a specific influence on both tympanic membrane, and to a lesser extent, oral temperatures that cannot be explained by generalized changes in core temperature. In Figure 10, by heating and cooling opposite sides of the face, tympanic membrane temperatures could be separated by as much as 0.4°C; yet when temperature changes common to both sides were performed, the two tympanic membrane temperatures showed similar changes. Figure 11 further demonstrates that, although tympanic membrane and oral temperatures could be changed by such maneuvers, aortic blood temperature, as indicated by esophageal temperature, remains essentially constant. When these observations are extended to include effect of head heating or cooling on face, scalp and neck, both tympanic and

oral temperatures followed the skin temperature on the ipsilateral side of the neck and head, in a manner similar to face heating. The possibility that temperature changes recorded on tympanic membrane are due to direct conduction from the surface skin is unlikely because of the total occlusion of the external auditory with a silicone rubber ear mold and the similar effects on tympanic membrane temperature seen from heating such regions as the face, scalp, and neck located at various distances from the tympanic membrane.

In Figure 13 and in various publications (7,10,155), decreases in esophageal, right atrial, tympanic membrane, and oral temperatures are often observed during rapid heating. This response appears to be due to increased venous return through tissue (e.g. skeletal muscle) that remains cool, increasing heat loss from the body core to the peripheral tissue.

Benzinger also noticed the influence of head skin temperature on tympanic membrane temperature. "In environments below 30°C, ear drum temperature changes perceptibly (0.1-0.2°C) when insulating material is placed upon or removed from the ear lobe and its surroundings. The lower readings prior to insulation are probably caused by cooler blood returning from the lobe and surrounding skin in descending veins adjacent to some of the ascending arteries which supply the tympanic membrane" (11). This explanation is inconsistent with his assumption that the blood supply is via the internal carotid artery unless this exchange occurs below the entrance of the internal carotid artery into the cranium.

Countercurrent heat exchange between the common carotid artery and venous blood draining the head has been suggested by Rubenstein et al (156). They observed a fall of 0.2 to 0.5°C in common carotid temperature when ice packs were applied to the "homolateral side of the anterior aspect of the face and forehead."

Marcus (157) has demonstrated that heating the head of a subject using radiant heat lamps can produce changes in ear canal temperature without changing esophageal temperature. He suggested this was due to a thermal exchange occurring in the region of the head. However, he was unable to produce consistent changes in ear canal temperature using small Peltier devices applied to the head or neck anywhere except just over the ear. No doubt the small surface area and difficulty in achieving good thermal contact with the rigid Peltier effect device prevented noticeable changes in ear canal temperature with the device on the top of the head or neck.

Similarities between tympanic membrane and hypothalamic temperatures in animals have been reported. Randall et al (151) showed that the tympanic membrane of cats is primarily heated by carotid blood while the hypothalamus is cooled by the carotid blood. Baker et al (139) showed good correspondence between tympanic membrane and hypothalamic temperatures during many physiological events. However, they reported that "the increase in ambient temperature had a more direct effect on tympanic membrane temperature than on hypothalamic." This observation has major implications on the usefulness of assessing hypothalamic temperature by measuring tympanic membrane temperature during externally applied heat stress involving the head.

It may be concluded that the temperatures of the tympanic membrane, oral cavity, and presumably other regions of the head are, in part, dependent on the thermal exchange demonstrated in the present work. This exchange must certainly involve the external carotid artery and perhaps the internal and common carotid arteries. The amount of exchange would be expected to differ from organ to organ, depending on the location of the heating or cooling of the skin, on the approximation of the supply artery with the returning blood from this area of the skin, on the relative blood flow, and on the skin temperature.

Thus, it would be presumptuous to assume that, during external heating of the head, temperature change in one part of the head would occur as rapidly or to the same extent as that in another part of the head. And, of course, it would be presumptuous to assume that tympanic membrane or oral temperatures demonstrate temperature changes identical to the hypothalamus when either the head or the entire body is heated or cooled. Since cranial temperatures, as assessed from the oral cavity and the tympanic membrane, are susceptible to modification by the local environment of the head, they will not represent central blood temperature accurately under conditions in which the head environment is drastically different from core temperature or when localized regions of heating or cooling are present on the surface of the head.

B. Effect of Skin Temperature On Sweating Rate (158,159)

The importance of skin temperature in the control of sweating in man has been disputed in the literature for some time. Benzinger et al (1) suggested that skin temperature had no effect on sweating as long as the skin temperature was above 33°C. This concept was supported by studies done by Brebner and Kerslake (2). The same year, Brebner and Kerslake (3) suggested that skin temperature influenced thermoregulatory sweating. These reports were followed by a series of observations that skin temperature was an important input to the thermoregulatory center and that skin temperature affected sweating rate, even at elevated temperatures (4-9).

More recently, however, it has again been suggested that skin temperature has an insignificant effect on sweating in man (10).

This controversy has been perpetuated by the experimental difficulty in separately controlling core and skin temperatures in a hot environment and by the lack of agreement over an appropriate measure of core temperature, especially during thermal transients.

Previous attempts to separate the effects of core and skin temperatures on sweating have used either exercise to change core temperature independently or rapid transients in environmental temperature to produce a change in skin temperature without a large amount of heat storage and a subsequent change in core temperature. Exercise is not ideal because it introduces an uncontrolled factor into the experimental procedure, and rapid changes in temperature make it necessary to record body temperature during nonsteady states.

An attempt was made in this study to achieve steady state changes in skin temperature without concomitant changes in deep body temperature. To keep body temperature constant during changes in skin temperature, the subjects drank cold (or warm) water to maintain a constant tympanic membrane temperature. Studies (described below) had demonstrated that this technique permitted control of deep body temperature during skin temperature changes.

1. Methods

Five male subjects (mean ht 178.4 cm, mean wt 87.4 kg, and mean DuBois area 2.0 m^2), clothed only in shorts, were used in a total of 30 experiments. They were heated or cooled by means of a specially constructed double-climate chamber, each half of which could be independently regulated (Fig 2). A movable bed in the chamber, equipped with a partition at waist level, permitted the subject to be placed completely in one chamber; the bed was then moved so that his legs and lower abdomen would be in the adjacent chamber at the same or different ambient temperature.

Temperature measurement. Skin temperature was measured on 12 regions using thermistors (Yellow Springs Instrument Co., YSI model 426): plantar foot (T_{pl}), dorsal foot (T_{do}), leg (T_{lg}), thigh (T_{th}), lower abdomen (T_{la}), upper abdomen (T_{ua}), lower chest (T_{lc}), upper chest (T_{uc}), palm (T_{pa}), forearm (T_{fa}), arm (T_{ar}), and forehead (T_{fh}). The thermistors were attached to the skin using a Plexiglas ring designed to maintain a constant contact pressure with the skin surface (4). Mean skin temperatures for the upper body ($\bar{T}_{SU}$) and lower body

($\bar{T}_{SL}$) were calculated using weighting formulas 1 and 2, based on the relative DuBois surface area of the body regions.

$$\bar{T}_{SU} = 0.14\ T_{fh} + 0.14\ T_{ar} + 0.14\ T_{fa} + 0.10\ T_{pa} + 0.16\ T_{uc} + 0.16\ T_{lc} + 0.16\ T_{ua} \quad (1)$$

$$\bar{T}_{SL} = 0.22\ T_{la} + 0.32\ T_{th} + 0.32\ T_{lg} + 0.07\ T_{do} \quad 0.07\ T_{pl} \quad (2)$$

Rectal temperature (T_{re}) was measured using a thermistor probe (YSI Model 401) introduced 10 cm beyond the anal sphincter. Tympanic membrane temperature (T_{ty}) was measured with a thermistor probe (YSI Model 520) inserted into the external auditory canal and held in place by a custom-made silicone rubber ear mold (148). The probe was inserted until definite contact was made with the tympanic membrane, as noted by a scratching sound, then fixed in place using a small clamp. This technique permitted positive contact of the thermistor with the tympanic membrane without discomfort.

Sweating measurement. Local sweating (S) was simultaneously measured on six body regions: forehead (S_{fh}), forearm (S_{fa}), chest (S_{ch}), abdomen (S_{ab}), thigh (S_{th}), and calf (S_{ca}). The sweating was measured by passing dried air at the rate of 0.5 l/min through capsules affixed to the skin and covering 9.8 cm^2 of skin area. The humidity of the air leaving the capsule was measured using resistance hygrometers (Panametrics). The hygrometers were kept in a constant temperature block at 41°C to prevent condensation and thermal drift (Fig 5). Calibration was done against a precision dew point hygrometer (Cambridge Systems, Model 880). Complete evaporation of water from the skin was

assured, since the relative humidity of the air leaving the collection capsule never exceeded 50 percent, even at the highest recorded sweating rate of 1 mg/min · cm^2. Complete evaporation was also confirmed by the rapid response of the hygrometry system to decreases in sweating rate. Such a response would depend on the rapid evaporation of water from the skin surface. The measured time delay of the system was five seconds.

Mean sweating rate for the whole body ($\bar{S}$), lower body ($\bar{S}_L$), and upper body ($\bar{S}_U$) were estimated using formulas 3, 4, and 5.

$$\bar{S} = (S_{fa} + S_{ch} + S_{ab} + S_{th} + S_{ca})/5 \quad (3)$$

$$\bar{S}_U = (S_{fa} + S_{ch} + S_{ab})/3 \quad (4)$$

$$\bar{S}_L = (S_{th} + S_{ca})/2 \quad (5)$$

Because of the difference in technique, these measurements cannot be considered equivalent to measured total body evaporative losses using gravimetric techniques, but they do provide an estimate of sweat gland activity over the body regions measured. S_{fh} was not used in the mean sweating calculations because of the limited area of this region.

Procedure. For each experiment the subject first sat quietly in one side of the double-climate chamber at a specified ambient temperature of 38°C for 1.5 hours. This period elevated the core temperature and established the activity of the sweat glands. After this equilibration period the instrumentation was put in place, and a 20 minute control period was recorded with the subject at the same ambient temperature. The lower body was then introduced into the adjacent chamber at a higher or lower ambient temperature for 20 minutes. The upper body, including the head, remained at the original temperature.

During this time the subject drank warm (45°C) or cold (10°C) water to maintain his T_{ty} at the initial level. The subject observed his own T_{ty} on a digital panel meter and drank water as necessary to maintain T_{ty} constant. With practice the subjects were able to maintain their T_{ty} within 0.1°C throughout the study. Depending on the subject and the thermal load, the quantity of water drunk was between 0.5 and 1.5 liters. The lower body was then returned to the chamber at the initial ambient temperature for an additional 20 minutes.

All measurements were recorded every 30 seconds by a scanning digital voltmeter (Vidar) and punched on paper tape. The data were later analyzed on a computer (PDP-12, Digital Equipment Corp.).

2. Results

Because the ability to maintain a constant core temperature by the drinking of cold or warm water is critical to the interpretation of the present study, several preliminary experiments were done to assess the validity of this procedure. Two subjects were used in these preliminary studies.

In the first study the subjects were equilibrated at 45°C ambient temperature. The lower body was then cooled in the adjacent chamber at an ambient temperature of 30°C. Warm water (45°C) was drunk to maintain T_{ty} constant for the next 20 minutes. The lower body was returned to an ambient temperature of 45°C for an additional 20 minutes. Finally, 1 liter of ice water was drunk rapidly (< 2 minutes), and the recording was continued for 20 minutes.

During lower body cooling there was an inhibition of sweating corresponding to the decrease in $\bar{T}_{SL}$ (Fig 14). During this period,

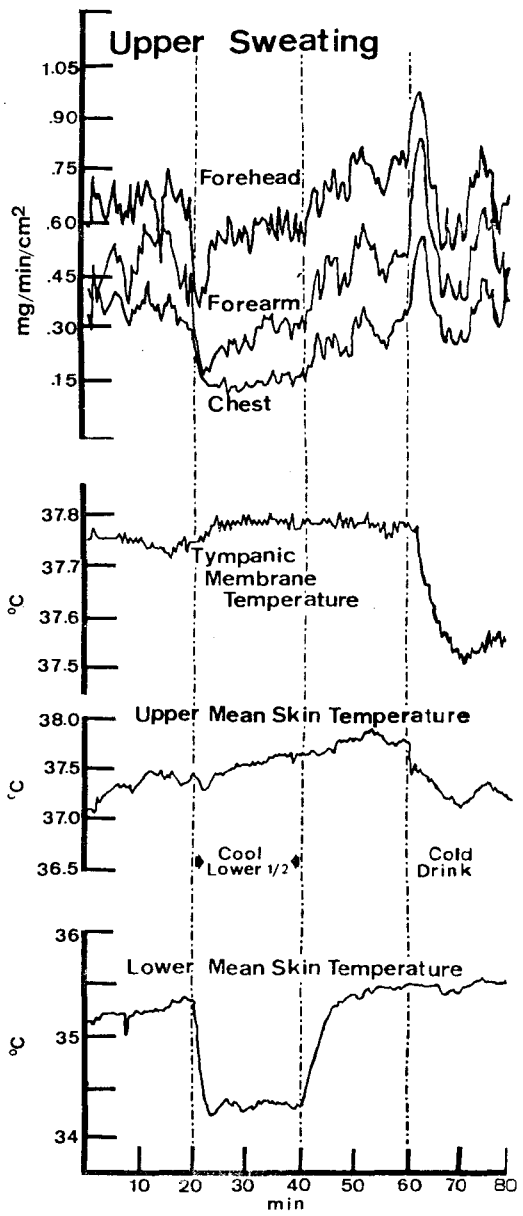

Figure 14. Responses of upper body sweating (forehead, forearm, and chest) to changes in lower body skin temperature during constant tympanic membrane temperature. Decrease in tympanic membrane temperature produced by rapid drinking of 1 liter of cold water (10°C) lowered the sweating rate at a constant skin temperature.

T_{ty} and $\bar{T}_{SU}$ did not decrease. During the initial cooling period there was a transient inhibition of sweating due to the dynamic properties of cutaneous thermoreceptors; however, steady state conditions were well established by the end of the 20 minute cooling period. Rewarming increased upper body sweating, corresponding to an increase in $\bar{T}_{SL}$ without a change in T_{ty}. During rewarming there was no evidence of dynamic augmentation of sweating. Rapid cooling of T_{ty} by the drinking of cold water reduced sweating, corresponding to the decreased T_{ty}. During cold water drinking there is a dynamic inhibition of sweating during the cooling of T_{ty}.

This study indicated that the drinking of warm water can be used to maintain T_{ty} constant during lower body cooling. It also indicated that T_{ty} measured during the drinking of cold water was a reliable estimate of core temperature because a decrease in T_{ty} due to water drinking produced the expected lowering in sweating rate while changes in skin temperature were minimal.

A second study was performed to determine if the drinking of cold water could control T_{ty} during lower body heating. The subjects were equilibrated at 35°C, followed by lower body heating in the adjacent chamber at an ambient temperature of 60°C. Cold water (10°C) was drunk to maintain T_{ty} constant. After 20 minutes the lower body was returned to the chamber at 35°C ambient temperature.

There was an increase in upper and lower body sweating, corresponding to the increase in $\bar{T}_{SL}$ during lower body heating (Fig 15). The drinking of cold water prevented an increase in T_{ty} during the heating period. At the end of the heating period, when the drinking

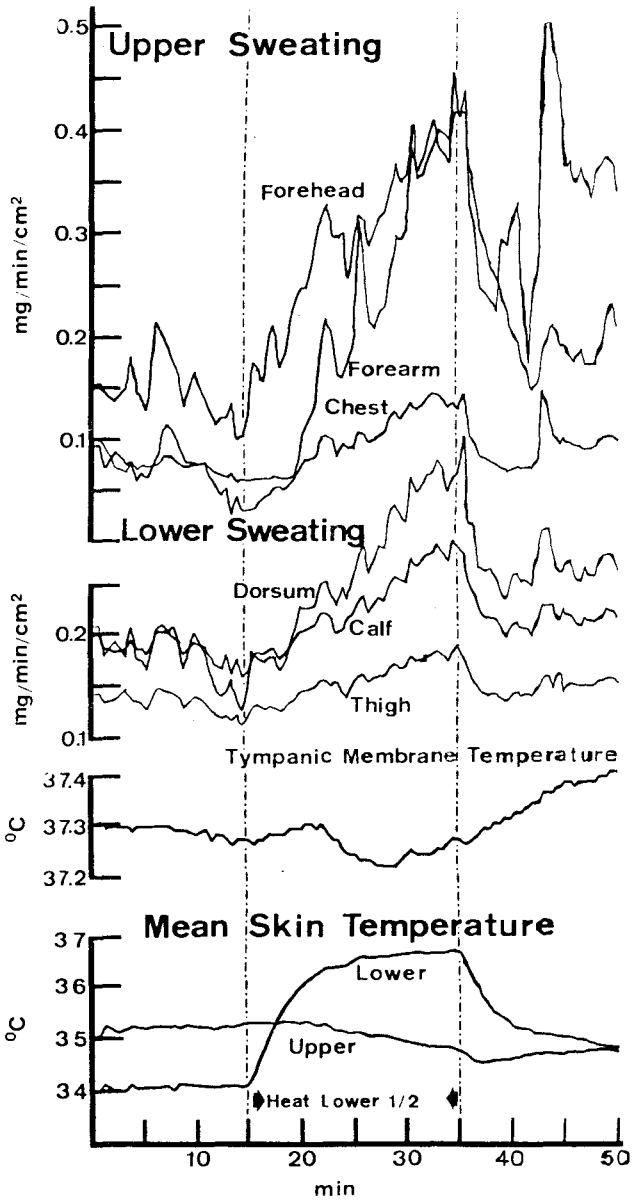

Figure 15. Responses of upper and lower body sweating to lower body heating while tympanic membrane temperature was maintained constant by drinking cold water (10°C).

of cold water was stopped, T_{ty} increased and there was a corresponding increase in sweating rate over both the upper and the lower body, while skin temperature remained constant.

This study confirms that the drinking of cold water maintains T_{ty} constant during lower body heating. The increase in sweating during the third period corresponds to the increase in T_{ty}, thus indicating that the expected relationship between T_{ty} and sweating rate is maintained.

Based on the results of these initial studies, five subjects were studied to determine the effect of skin temperature on sweating at constant core temperature. The subjects were equilibrated at an ambient temperature of 38°C. The lower body was then placed into the adjacent chamber at an ambient temperature of 29, 38, 50, 60, 70, and 80°C for the next 20 minutes. During the period the subjects maintained T_{ty} constant by drinking cold (or warm) water. The lower body was returned to the 38°C chamber for the final 20 minutes of the study. The subject was not told of the temperature of the adjacent chamber before the study, and the sequence of performing the experiments was random.

Representative recordings from one subject--a composite of three experiments during which the lower body was exposed to ambient temperatures of 50, 60, and 70°C--shows that, during the control period at an ambient temperature of 38°C, S_{fa} remained approximately 0.1 mg/min $\cdot$ cm^2 (Fig 16). After the lower body was heated, S_{fa} increased, corresponding to the increase in $\bar{T}_{SL}$. By drinking cold water the subject maintained a constant T_{ty}, and there was minimal (< 0.5°C) change

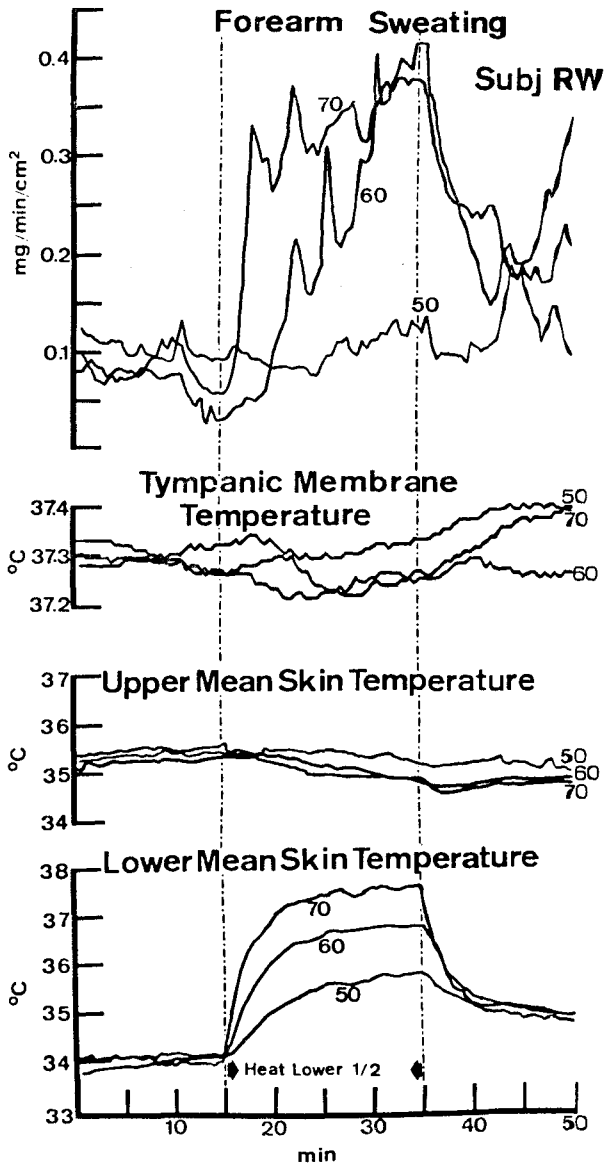

Figure 16. Results of three experiments on subject RW. Lower body was heated in three ambient temperatures (50, 60, and 70°C) while upper body was maintained at ambient temperature of 38°C. Forearm sweating increased with mean lower body skin temperature ($\bar{T}_{SL}$) while tympanic membrane temperature (T_{ty}) was maintained constant by the drinking of cold water (10°C).

in T_{re} during the study. $\bar{T}_{SU}$ tended to decrease slightly during the heating of the lower body. This decrease was due to evaporative cooling secondary to the increased sweating rate of the upper body during this time period.

The results of the study were condensed by calculating $\bar{S}$, $\bar{S}_U$, and $\bar{S}_L$ from the local sweating rates recorded on the five body regions. The mean sweating rates were calculated for the last five minutes of the lower body heating (or cooling) period. These mean sweating rates were used to calculate the sensitivity of sweating to changes in skin temperature.

$\bar{S}$ was plotted against $\bar{T}_{SL}$ for each subject, and a regression of coefficient was calculated (Table 1). The sensitivity of $\bar{S}$ to the changes in $\bar{T}_{SL}$ varied between subjects. The lowest was 0.03 mg/min · cm^2 · °C, and the highest was 0.09 mg/cm^2 · min · °C. Each of these regression coefficients (β) was significantly different from zero ($P < 0.05$, Student's t test). Because the regression coefficients were not significantly different between subjects ($P > 0.05$, analysis of covariance), the subject data were pooled (Fig 17).

The lower body was exposed to varied ambient temperatures, while the upper body was maintained at an ambient temperature of 38°C in all cases. Because experimental evidence suggests that local temperature can affect sweat gland output, the regression of both $\bar{S}_L$ and $\bar{S}_U$ on $\bar{T}_{SL}$ was calculated (Fig 18,19). There was no significant differrence between the slopes of these regression lines ($P > 0.05$, Student's t test). This does not indicate, however, that the local temperature has no effect on sweating rate, because the sensitivities of the upper

TABLE 1

REGRESSION COEFFICIENTS FOR MEAN SWEATING RATE

ON LOWER BODY MEAN SKIN TEMPERATURE

Subject	β, $mg/cm^2 \cdot min \cdot °C$	T_{ty}, °C	T_{re}, °C
RW	0.068 ± 0.009	37.32 ± 0.033	37.15 ± 0.071
SG	0.054 ± 0.020	37.19 ± 0.087	37.01 ± 0.105
TM	0.075 ± 0.017	37.37 ± 0.122	37.11 ± 0.119
KJ	0.035 ± 0.004	37.11 ± 0.094	37.05 ± 0.084
DE	0.091 ± 0.011	37.37 ± 0.123	37.26 ± 0.172
Mean	0.069 ± 0.007	37.27 ± 0.052	37.12 ± 0.043

Values are means ± SE; n = 5. β, regression coefficient; T_{ty}, tympanic membrane temperature; T_{re}, rectal temperature.

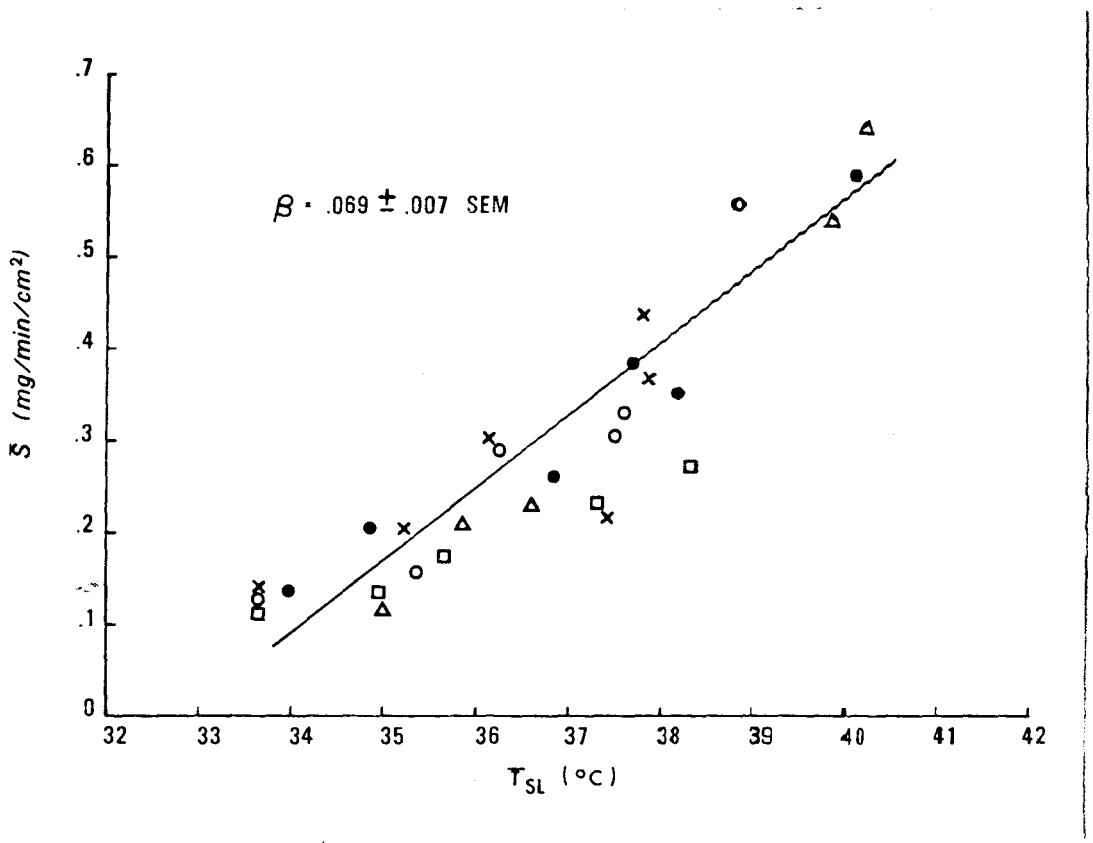

Figure 17. Responses of $\bar{S}$ to $\bar{T}_{SL}$ in each of five subjects (closed circle, RW; cross, SG; open circle, TM; open square, KJ; open triangle, DE). There was no apparent significant difference between slopes of (β) of the regression lines ($P > 0.05$). Pooled data and mean regression lines are shown.

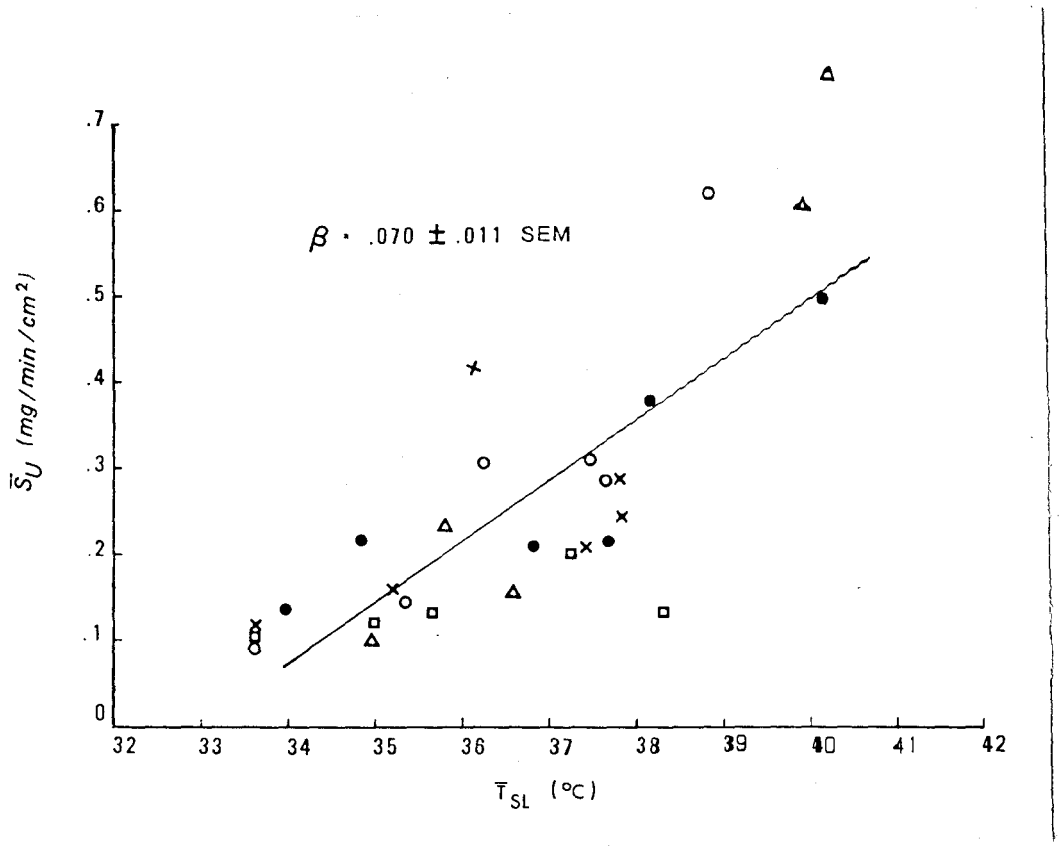

Figure 18. Regression line of $\bar{S}_U$ on $\bar{T}_{SL}$ (closed circle, RW; cross, SG, open circle TM; open square, KJ; open triangle, DE).

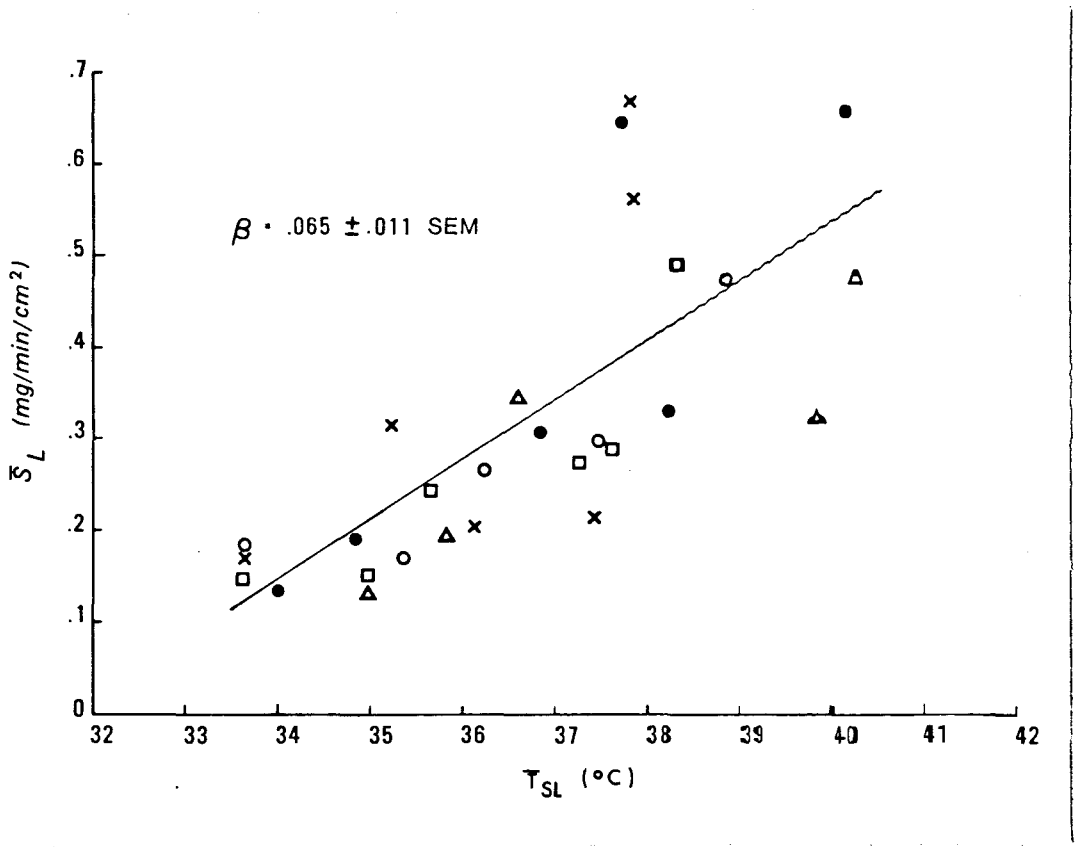

Figure 19. Regression of $\bar{S}_L$ on $\bar{T}_{SL}$. There is no significant difference between slopes (β) of the regression line in this figure and in Figure 17 ($P > 0.05$) (closed circle, RW; cross, SG; open circle, TM; open square, KJ; open triangle, DE).

and lower body to thermoregulatory stimuli are known to be different (155).

3. Discussion

This investigation demonstrates that changes in skin temperature of one body segment can change the sweating rate of another region of the body even at elevated skin temperatures. It also indicates that this change in sweating rate must be mediated by neural input to the thermoregulatory center, because there was a regulation of sweating on the upper body during stimulation of the lower body while cutaneous and core temperatures of the upper body remained constant.

Both T_{ty} and T_{re} were used as estimates of core temperature, and care was taken to assure that the measurements were reliable estimates of core temperature. First, the measurement of T_{ty} was made while the head and upper body were in a warm environment (38°C), approximately that of deep body temperature. Maintaining the skin temperature of the head near core temperature made it unlikely that T_{ty} would be influenced by cooled blood draining from the skin of the head surrounding the external auditory canal (11). Second, the use of cold water to maintain the core temperature constant assured not only that any change in sweating rate was due to changes in skin temperature, but also that transients in T_{ty} would be eliminated. Since T_{ty} and T_{re} remained essentially constant throughout the studies, T_{ty} paralleled blood temperature and perhaps hypothalamic temperature, because any differences in the time constants of these temperatures to thermal transients were eliminated.

Although in severely dehydrated persons subjected to prolonged heat stress the drinking of water increases sweating rate (161), the subjects in this study were well hydrated before the beginning of the experiment and the thermal stress was not prolonged. Thus, in control experiments during which water was drunk while skin temperature remained constant there was no increase in sweating rate.

The drinking of water that is colder or warmer than deep body temperature might stimulate deep body thermoreceptors, as described by Rawson and Quick (65-70). If this had occurred in the present study, changes in sweating would have occurred before the changes in T_{ty}. However, when cold water was rapidly drunk, the decrease in sweating did not precede the decrease in T_{ty} (Fig 13). Although deep body thermoreceptors may be present in man, they are not preferentially stimulated by the water-drinking maneuvers of the study.

Wyss et al (10) suggested that skin temperature has an insignificant effect on sweating rate. They argued that the previous reports supporting the effect of skin temperature on sweating rates were due to the time lag in the measurements of core temperature used by the investigators who showed an effect of skin temperature on sweating rate. In their studies using right atrial temperature as a measure of core temperature, Wyss et al (10) found that skin temperature had an insignificant effect on sweating rate. Because they did not control skin temperature and core temperature independently, they performed multiple linear regression to determine the relative effects of skin temperature and core temperature on sweating rate. This procedure is complicated by the high correlation between skin temperature and core

temperature in a warm environment, thus making it diffcult to isolate a causal relationship to one of the factors and not the other, even when statistical significance is demonstrated for only one factor.

Wyss et al did not find an effect of skin temperatures on sweating, probably because they began their temperature changes with a core temperature that was low (36.5°), and because they did not prime the subjects to initiate a steady state of sweating. A delay in initiating sweating would minimize the observed effect of skin temperature on sweating rate.

In the present study core temperature, as determined by T_{ty} and T_{re}, was maintained at a constant level throughout the experiment. This permitted regression analysis to be performed against a single changing variable, $\bar{T}_{SL}$. By maintaining T_{ty} and T_{re} constant, the problem of time lags in the measurements also was eliminated.

Because core temperature measurements as determined by T_{ty} and T_{re} remained essentially constant for at least 20 minutes, any transient temporal difference between deep body temperatures should be eliminated. Although both T_{ty} and T_{re} are only estimates of core temperature, presumably hypothalamic temperature and other deep body temperatues also should remain constant under these circumstances.

Using a procedure similar to the one described, Brebner and Kerslake (2) showed, contrary to our results, that leg cooling had no effect on the sweat rate of the forearm. However, to prevent a decrease in core temperature during leg cooling, they occluded the arteries of the legs. Because leg cooling in their experiments was effective in altering sweating rates before occlusion but not after,

an alternative explanation for the lack of response after occlusion could be the detrimental effect of ischemia on the thermoreceptors of the legs (162), a factor that they recognized (3).

The present study confirms the concept of a proportional control of sweating at high (> 33°C) as well as low skin temperatures. The earlier work by Nadel et al (5) estimated that the regression coefficient for sweating relative to skin temperature (β) was approximately 0.14 $mg/cm^2 \cdot °C$. This agrees well with our observed value of 0.069 for half-body heating and cooling. Because only one-half of the body surface was heated or cooled in our study, the control coefficient should be twice the observed slope of $\bar{S}$ versus $\bar{T}_{SL}$. This close agreement of the effect of skin temperature on sweating in two technically dissimilar studies suggests that inaccurate measurements of core temperature were not the cause of the observed effect of skin temperature on sweating in the work of Nadel and others.

Although there was no significant difference between the regression coefficients of $\bar{S}_L$ versus $\bar{T}_{SL}$ and $\bar{S}_U$ versus $\bar{T}_{SL}$, this does not imply that no local temperature effect on sweating rate was present. $\bar{S}_U$ was determined by thermoreceptor activity alone whereas $\bar{S}_L$ was determined by thermoreceptor activity and local temperature effect on the sweat glands. It is fortuitous that the regressions of $\bar{S}_L$ and $\bar{S}_U$ on $\bar{T}_{SL}$ were equal, the local effect on $\bar{S}_L$ being balanced by a slightly greater sensitivity of $\bar{S}_U$ to thermoreceptor activity. The design of this study did not permit the sensitivity of $\bar{S}_L$ to thermoreceptor activity alone to be determined.

Fundamental questions remain concerning the mode of interaction of central warm receptors and peripheral receptors in initiating and sustaining thermoregulatory sweating in man. The simplest assumption is that peripheral thermoreceptor input and central thermoreceptor input are additive. However, there is experimental evidence in several animal species of a multiplicative relationship between hypothalamic temperature and skin temperature in producing the thermoregulatory signal (68,94,95).

In the present investigation the validity of the additive or multiplicative models cannot be resolved since deep body temperature was "clamped" at a constant temperature to demonstrate the effect of skin temperature alone on sweating rate. For this reason, the interaction of deep body temperature and skin temperature could not be determined.

C. Effect of Head Heating and Cooling on Sweating in Man (163)

In experiments to determine effective means of reducing the stress of exposure to high environmental temperatures, it has been shown that head cooling can greatly reduce thermal discomfort and improve performance (144-147). Evidence has been presented that this reduction in thermal discomfort and thermal stress is due to the reduction in total body heat load by the dissipation of heat from the highly vascular cutaneous regions of the head (146,147). The head appears to be particularly suited for this function because of the resistance of its extensive cutaneous circulation to vasoconstriction during cooling. The data of Williams and Shitzer (147), indicated that from 10 percent to 30 percent of the total metabolic heat produced could be removed by head cooling.

It has also been shown by Crawshaw et al (164) that head cooling is more effective than regional cooling of other body surfaces in reducing sweating. They suggested that the high efficacy of head cooling in reducing sweating rate was due to the high concentration of thermoreceptors, especially cold receptors in the facial and head regions.

These suggestions help to explain the great influence of head skin temperature in human thermoregulation. However, another factor may contribute to the unique role of the head in thermoregulation in man. The work of Marcus (135,157) has indicated that tympanic membrane temperature and oral temperature are particularly affected by heating or cooling quite localized areas of skin on the head, face, and neck. A

countercurrent thermal exchange occurring in the neck between the carotid arterial blood ascending to intracranial structures and venous blood draining the cutaneous regions of the head, face, and neck may be responsible for the effect of head and neck heating on tympanic membrane temperature. This thermal exchange was shown by changes in tympanic membrane and oral temperatures during head heating and cooling while esophageal temperature remained essentially unchanged (150).

Such a system of thermal exchange between venous blood draining the head and arterial blood ascending to intracranial structures, including the hypothalamus, has been demonstrated in the sheep (142), dog (165), and rabbit (166).

The following experiments were undertaken to determine if a thermal countercurrent exchange is a factor in altering thermoregulatory sweating in man during isolated head heating and cooling.

1. Methods

Three male subjects (Table 2) wearing only shorts were used in a series of experiments involving independent heating and cooling of the head while the rest of the body remained at a constant ambient temperature. Heating and cooling were done in a specially constructed double climate chamber which permitted independent regulation of the temperature in the adjacent rooms. The subject lay supine on a bed which could be rapidly moved from one room to the other. An insulating diaphragm was placed on the bed at neck level. This system allowed for equilibration of the subject in one chamber at an ambient temperature of 40°C followed by movement of the bed to introduce the subject's head and neck into the adjacent chamber at an environmental temperature

TABLE 2

PHYSICAL CHARACTERISTICS OF THE SUBJECTS

Subject	Ht(cm)	Wt(kg)	Area(m^2)
TVM	180	79.5	1.99
GSG	168	68.2	1.77
JMC	169	63.0	1.75
Mean	172	70.2	1.84

of 70°C or 29°C. The vapor pressures in the chambers at 40°, 70°, and 29°C were 10.8, 11.0, and 9.7 mm Hg, respectively. Vapor pressure in these three environments did not limit cutaneous evaporative cooling.

Before the experiment the subject would sit quietly in the chamber at an ambient temperature of 40°C for 1 to 1.5 hours; this elevated core temperature and initiated a moderate degree of sweating. Temperature and sweat measuring instruments were then attached to the subject and a ten-minute control measurement was made. Next, the bed was moved in order to introduce only the subject's head into the adjacent chamber, which was regulated at a temperature of 70°C for head heating or 29°C for head cooling. The subject remained in this position for 30 minutes and was then returned to the 40°C chamber for an additional 20-minute recovery period. The temperatures of 70°C and 29°C for head heating and cooling were selected to produce a considerable change in head skin temperature without producing pain which would have had unpredictable effects on sweating rate.

Temperature recording. Skin temperature was recorded from nine body regions using matched thermistors (YSI Model 421). The regions were dorsum of the foot (T_{do}), calf (T_{ca}), thigh (T_{th}), abdomen (T_{ab}), chest (T_{ch}), arm (T_{ar}), forearm (T_{fa}), palm (T_{pa}), and forehead (T_{fh}). Mean skin temperature ($\bar{T}_{sk}$) was calculated from the weighted average of the nine skin areas according to Equation 1 (167).

$$\bar{T}_S = .07T_{do} + .13\ T_{ca} + .19\ T_{th} + .15\ T_{ab} + .20\ T_{ch} + .07\ T_{fh} + .07\ T_{ar} + .07\ T_{fa} + .05\ T_{pa} \quad (1)$$

Deep body temperature was measured from the rectum, esophagus, oral cavity, and tympanic membrane. Rectal temperature was measured

with a thermistor probe (YSI Model 401) introduced 10 cm beyond the anal sphincter. Esophageal temperature was measured with a thermistor probe (YSI Model 401) introduced through the nose and down the esophagus to the level of the left atrium as determined by roentgenological examination. The probe was then secured with tape. The oral temperature was measured by a thermistor probe (YSI Model 421) held under the tongue near the lingual artery. The tympanic membrane temperature was measured using a very small thermistor probe of 1 mm diameter (YSI Model 520) introduced through a custom silicone rubber ear mold (143) until positive contact was made with the tympanic membrane, as evidenced by a sharp scratching heard by the subject. This probe was held in place by a small clamp. To assure that ambient temperature had no direct effect on the tympanic membrane thermistor, the ears were further insulated with a protective headset. This headset covered the external ears completely and was heavily insulated to prevent the direct heating of the thermistor lead introduced into the ear or of the pinna of the ear and surrounding skin.

Sweating measurement. Sweating was measured on six body regions: the calf (S_{ca}), thigh (S_{th}), abdomen (S_{ab}), chest (S_{ch}), arm (S_{ar}), and forearm (S_{fa}). Mean sweating ($\bar{S}$) was calculated according to Equation 2.

$$\bar{S} = .04\ S_{ar} + .05\ S_{fa} + .22\ S_{ch} + .22\ S_{ab} + .25\ S_{th} + .22\ S_{ca} \qquad (2)$$

The constants are derived from the measured percentage of total body sweating expected from the region as determined by Hertzman et al (160).

The sweat recording apparatus is diagrammed in Figure 5. Sweating was determined by passing dry air at a measured flow rate (0.5 L/min in these experiments) over the skin using specially constructed capsules which covered an area of 9.8 cm^2. The air was then passed through resistance hygrometers (Panametrics) which had been calibrated against a precision dew-point hygrometer (Cambridge Systems Model 880). The hygrometers were maintained in a constant temperature block to prevent thermal drift, and the system had a measured delay of five seconds due to the length of the connecting tubing.

Data collection. All skin core and ambient temperatures, as well as hygrometer readings, were scanned at 30 second intervals, digitized, and recorded on paper tape in BCD format for later analysis on a PDP-12 computer (Digital Equipment Corp.). The analysis consisted of calculating mean temperatures and sweating rates, averaging experimental results and plotting the data.

2. Results

Figure 20 shows the results of an experiment in which the subject's head was heated in an environmental temperature of 70°C while the rest of the body was maintained at an ambient temperature of 40°C. During the initial ten-minute control period, all temperatures were stable and mean sweating rate showed typical oscillations at the rate of approximately one every two minutes. When the subject's head was rapidly shifted into the 70°C environmental chamber, there was an immediate and rapid rise in head skin temperature. Rectal temperature remained stable during most of the heating period with a slow rise near the end of the 30-minute heating period. Esophageal temperature showed

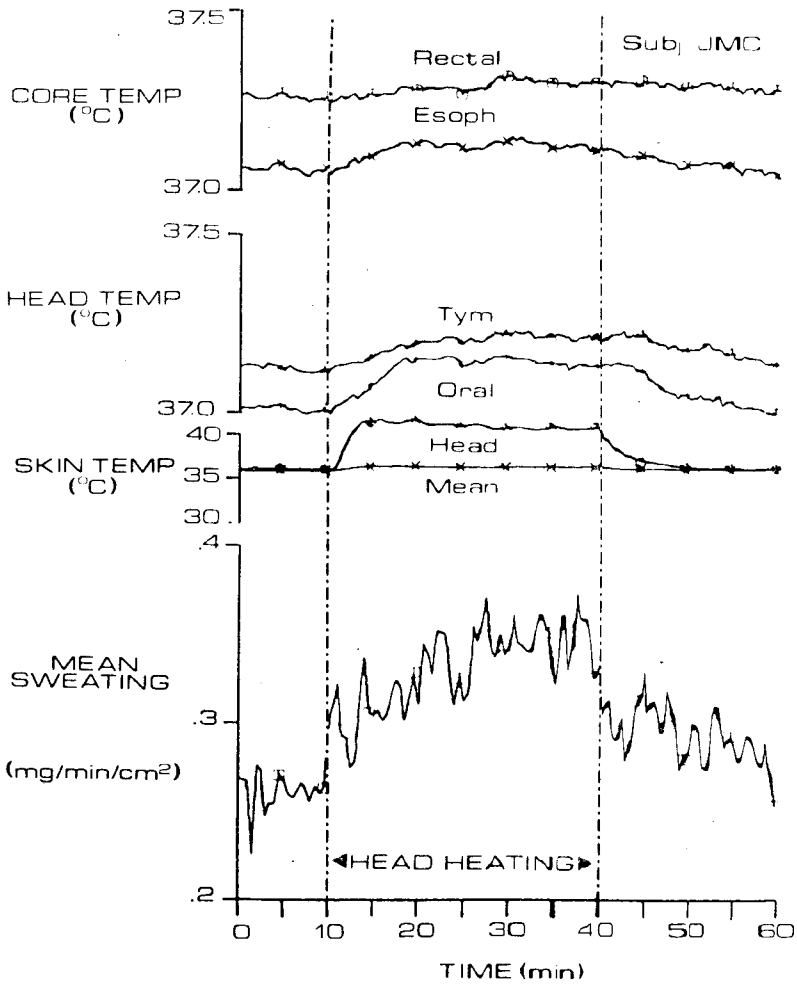

Figure 20. The response of subject JMC to isolated head heating in an ambient temperature of 70°C. Deep body temperatures shown are rectal, esophageal, tympanic membrane, and oral. Head skin temperature, mean skin temperature, and mean sweating rate are shown in the lower part of the figure.

a gradual rise during the heating period, but it was less than the increase in either tympanic or oral temperature which began to rise soon after the initiation of heating. Mean sweating showed a rapid rise as head skin temperature increased and a slower progressive rise during the remainder of the heating period while tympanic membrane and oral temperatures were rising.

At the termination of heating the course of events was reversed. Rectal temperature remained stable, and esophageal temperature showed a slow decline. Tympanic and oral temperatures again showed a more marked decline than either rectal or esophageal temperatures. The sweating rate showed an initial rapid fall during the rapid skin cooling, then a slower decline toward control levels as tympanic membrane and oral temperatures fell.

In Figure 21, the results of a head cooling experiment on another subject are shown. In this experiment, the subject's head was cooled in an environmental temperature of 29°C while the rest of the body was maintained in an ambient temperature of 40°C. During the period of head cooling, neither rectal nor esophageal temperature showed any consistent changes. Tympanic and oral temperatures both showed a progressive decline during the head cooling followed by a rise during the recovery period. Sweating rate showed a slow decline during the cooling period followed by a rise during recovery. In this case changes in sweating rate were clearly not related to changes in either rectal or esophageal temperature, and appeared to be related to some combination of head skin, oral, and tympanic temperatures.

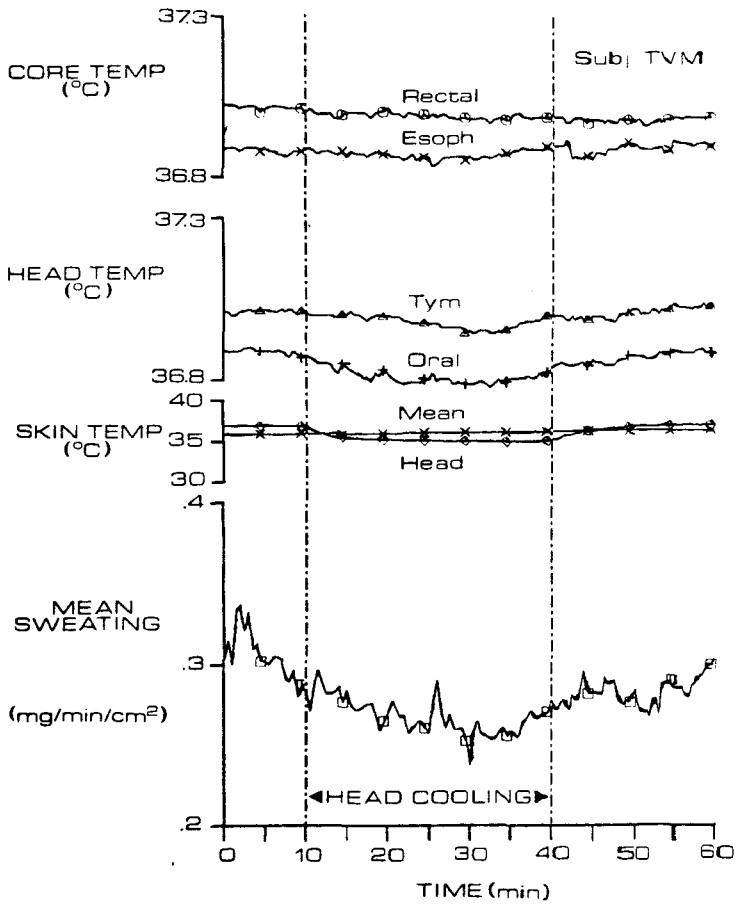

Figure 21. The response of subject TVM to isolated head cooling in an ambient temperature of 29°C. Measurements are as in Figure 20.

To simplify the presentation of the results on the whole series of experiments, the data have been combined in the following manner:

The effect of head heating and cooling on the deep body temperatures was taken to be the maximum change in each of the deep body temperatures during heating and cooling of the head from the average temperature during the initial ten-minute control period. The means of the maximum temperature changes for each of the deep body regions are shown in Figure 22 with standard errors. In order to represent concisely the effect of head heating and cooling on sweating rate, the change in total amount of sweat produced during the last 50 minutes of the experiment from that expected from the mean sweating rate during the initial ten-minute control period was calculated. This value should represent the total effect of the head heating and cooling on the sudomotor activity. The mean value for change in sweating is given in Figure 22 along with the maximum changes in deep body temperatures. This figure shows that rectal temperature is only slightly affected by head heating and cooling, and that esophageal temperature is altered by head heating and cooling but not to the same degree as tympanic membrane and oral temperature. The figure also shows the increase in sweating rate during head heating and the decrease during head cooling. Due to the small number of observations, it is difficult to demonstrate statistical differences between the changes in the various core temperatures, although the changes showed the same pattern in each of the subjects tested. However, if the data for both heating and cooling the head are pooled using the absolute value of

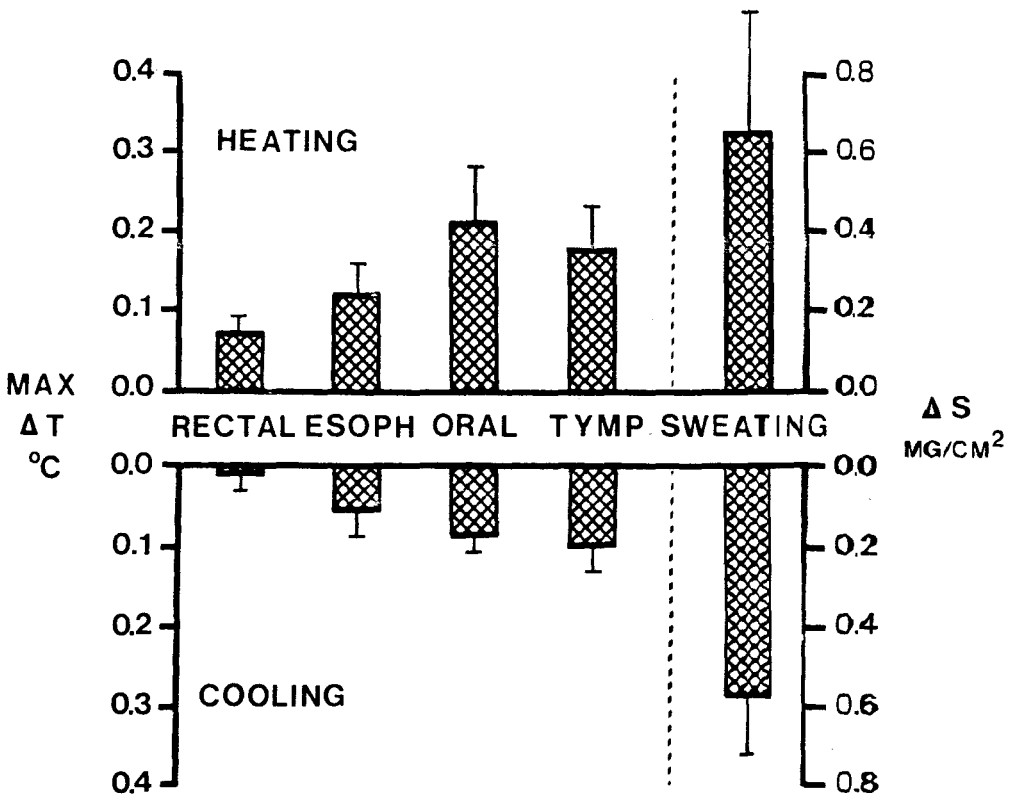

Figure 22. Maximal changes in deep body temperatures during head heating (upper) and head cooling (lower) for the three subjects. Total change in sweat produced for the experimental period from control level is shown on the right. The crossed thin bars represent standard errors of the mean.

the change in deep body temperature, a Student's t test for significance shows no significant change in rectal temperature during head temperature changes ($p > 0.05$), while there are significant changes in the other deep body temperatures and sweating rate. Using a Student's t test to compare deep body temperatures shows a significant difference ($p < 0.05$) between rectal temperature change and changes in tympanic and oral temperatures but no significant difference between rectal temperature change and change in esophageal temperature during head skin temperature changes.

3. Discussion

Hayward and Baker (168) have shown that, in the monkey, hypothalamic temperature is closely related to arterial blood temperature. Any deep body temperature, including esophageal, rectal, oral, or tympanic membrane temperature, that is a reliable estimate of arterial blood temperature can, therefore, be considered a reasonable estimate of hypothalamic temperature under most conditions. This assumes, however, that there is no change in blood temperature from the time it leaves the great vessels until it reaches the hypothalamus. Baker et al (139-143) have shown in animal species with a carotid rete that arterial blood cooling occurs in the rete due to a countercurrent thermal exchange between the venous blood draining the head and the arterial blood. This thermal exchange may serve to protect the sensitive brain from excessive heating during thermal stress. Although this exchange is most notable in animals with a carotid rete, such as the sheep and dog, it has also been shown to occur in the rabbit (166), an animal without a carotid rete. Brain temperature in these animals in which

countercurrent thermal exchange occurs cannot be determined from measurements of arterial or deep core temperature, since the brain temperature depends on the cooling occuring in the carotid rete.

Although man does not have a carotid rete to facilitate thermal exchange between venous blood draining the head and arterial blood ascending to the hypothalamus, there is an anatomical basis for thermal exchange between arterial and venous blood in the neck. Figure 8 shows the close relationship between veins draining the scalp, face, and neck, and the common and internal carotid arteries. Due to the high diffusing capacity of heat, some thermal exchange is likely to occur in this region.

The work of Marcus (135,157) have demonstrated that changes in heating applied to localized regions of the neck, face, and scalp produced a change in tympanic and oral temperatures--regions above the site of thermal exchange--while esophageal temperature remained essentially unchanged. However, heating applied to the legs produce temperature changes in all deep body locations. These data are further supported by the findings of Rubenstein et al (156), who recorded changes in carotid arterial blood temperature during heating of the neck and scalp during carotid angiography. Together, this evidence would suggest that a thermal countercurrent exchange does occur in the cervical region in man.

If it is to be suggested that the described thermal countercurrent exchange is of thermoregulatory significance in man, it must be shown that thermosensitive sites are influenced by the heat exchange. The major thermosensitive location in the head is the hypothalamus, but

since the hypothalamus is not accessible for measurement in man, an indirect approach is necessary to evaluate hypothalamic temperature.

The present investigation supplies further supportive evidence that a thermal countercurrent exchange influences thermoregulation in man. Since skin temperature and hypothalamic temperature are the most important factors determining sweating rate, if skin temperature is maintained constant sweating rate will indicate changes in hypothalamic temperature. In these experiments, when head skin temperature was abruptly changed, a corresponding change in sweating was associated with the rapid change in cutaneous thermoreceptor activity. The results of the experiments showed a slow change in sweating rate after the initial skin temperature change. These sweating changes also corresponded most closely to deep head temperature measurements, tympanic and oral. This suggests but does not prove that the same countercurrent exchange which is known to produce changes in tympanic and oral temperature, also influences the hypothalamic temperature, and thus the thermoregulatory effector mechanisms.

A thermal exchange mechanism, as is suggested by the data, would have several important effects on adaptation to hot environments and on the efficacy of head cooling in improving thermal comfort and performance in hot environments. If the head is cooled during thermal stress, either by natural means such as evaporation or by forced cooling, deep cephalic structures including the brain would be preferentially cooled while the other deep internal organs would retain the stored heat. This would protect the brain from excessive heat stress. This mechanism would help explain the high efficiency of head cooling

in reducing stress and increasing performance in hot environments as has been demonstrated by other workers (144-147).

The ability of the cutaneous circulation of the head to resist vasoconstriction to cold and to dissipate large amounts of heat (169) combined with the selective removal of heat from intracranial structures could be important in survival in hot environments.

The data also indicate that during head heating deep body temperature measurements made at the rectum or esophagus may underestimate the deep body temperature sensed by the hypothalamus. Such a situation would cause an overestimate of the effect of head skin temperature on sweating or thermal comfort.

In conclusion, this work offers supportive evidence for a thermal countercurrent exchange in the cervical region in man which is effective in altering sweating rate. This exchange may function in man to maintain brain temperature during exposure to thermal stress. Such a mechanism may offer an additional explanation for the efficacy of head cooling in reducing thermal stress and improving performance in hot environments.

V. GENERAL DISCUSSION

The investigations presented demonstrate that changes in skin temperature of one body region can change sweating rate of another body region. Two distinct mechanisms for the regulation of sweating by skin temperature are presented; 1) changes in sweating induced by changes of thermoreceptor input from the skin independent of changes in deep body temperature (Investigation 2), and 2) changes in sweating rate induced by changes in skin temperature in a specialized body region, the head. In this case, there is evidence that sweating rate is affected not only by changes in thermoreceptor input from the skin of the head; but, in addition, by selective changes in hypothalamic temperature produced by a countercurrent heat exchange between blood draining the highly vascular scalp and face skin and the arterial blood supplying the intracranial structures (Investigations 1 and 3).

Both these mechanisms of thermoregulatory sweating control are controversial. It is generally accepted that changes in skin temperature in a cool environment affect sweating rate; however, Benzinger (11) had suggested that skin temperature had no affect on sweating rate above a temperature of 33°C. This argument was supported by Brebner and Kerslake (2) and later Wyss et al (10), although other groups have demonstrated that skin temperature does affect sweating rate even at elevated temperatures (3-9).

The most important reason for the controversy is the inability to produce a constant deep body temperature in a warm environment during changes in skin temperature.

To produce such changes, previous investigators have either produced abrupt changes in skin temperature by intense heating or cooling and making measurements during the transients produced (7), or stabilized deep body temperature by exercise (170). These methods both have disadvantages, the first in producing non-steady state conditions in which the dynamic response of cutaneous thermoreceptors become important and the second in introducing exercise as an uncontrolled variable.

In the present study a third alternative was utilized. Deep body temperature was maintained by the controlled drinking of warm and cold water. The high heat capacity of water assured a relatively great stability of temperature. The feasibility of this technique was demonstrated.

Under steady state conditions of deep body temperature in which skin temperature was varied over a wide range of temperatures from thermoneutral to 80°C, cutaneous thermoreceptors were shown to have a definite influence on sweating in regions of the body not subjected to local temperature changes. This phenomenon is consistent with a neurally-mediated effect of cutaneous thermoreceptors on the thermoregulatory center under steady state conditions in a hot environment.

The second mechanism proposed for cutaneous regulation of thermoregulatory sweating is the indirect effect of head skin temperature upon brain and specifically hypothalamic temperature by means of countercurrent head exchange.

Modification of brain temperature by a countercurrent heat exchange mechanism is known to occur in animals possessing a carotid

rete (138-143). In these animals arterial blood is cooled immediately before it enters the brain by close contact with cool venous blood returning from the nasal cavity and exposed regions of the head. Even in animals without a carotid rete, some brain cooling occurs (166).

It has been assumed that in the human no such thermal countercurrent exchange occurs between venous blood leaving the head and arterial blood supplying the brain. However, it has been noted that cooling the head is particularly effective in improving performance of heat stressed humans (144-147). In addition, it has been shown by Crawshaw, Nadel, Stolwijk and Stamford that local cooling of the head inhibits sweating twice as effectively as cooling other body regions of comparable size (164).

These two observations suggest that perhaps head skin temperature may modify hypothalamic temperature and thereby modify the thermoregulatory controller by a counter-current heat exchange mechanism.

Proving this hypothesis is frought with technical difficulties foremost of which is measuring hypothalamic temperature in the human subject. Since direct measurement is out of the question except in the course of neurosurgical procedures, the present study selected two estimates of hypothalamic temperature to determine the influence of head skin temperature on brain temperature.

In Investigation 1, tympanic membrane temperature was utilized as an estimate of brain temperature. Tympanic membrane temperature was originally suggested by Benzinger (11) as the best estimate of hypothalamic temperature. In this investigation, it was apparent that selective cooling or heating of the head or neck could influence tympanic

membrane temperature without changing deep body temperature. If, in fact, tympanic membrane temperature is a reasonable estimate of brain temperature, skin temperature did have a direct influence on hypothalamic temperature.

Such an assumption was considered unverifiable so an alternative indirect measure of brain temperature was selected. In this case, it was the sweating rate under conditions of constant skin and deep body temperature. In Investigation 3, subjects were kept at a constant body temperature during selective heating and cooling of the head. The sweating rate changes observed in response to head heating corresponded more closely to tympanic membrane and oral temperature than to rectal or esophageal temperature. Since esophageal and rectal temperature could be considered to be measures of blood temperature, it can be argued that the thermoregulatory controller temperature and therefore, hypothalamic temperature was changing while blood or deep body temperature remained constant. The sweating response to selective head heating and cooling can be accounted for by proposing a thermal countercurrent exchange between the head skin and the arterial blood supplying the intracranial structures.

More recently, Cabanac and Caputa (171) have confirmed our original observations and supplied more evidence that indeed such a selective brain temperature regulating system exists in man. Although the magnitude of the thermal countercurrent exchange between venous and arterial blood in the head of the human is not comparable to the efficient mechanism present in animals with a carotid rete, it may be important

under conditions of heat stress especially during exercise when skin temperature may be considerably lower than arterial blood temperature.

VI. CONCLUSIONS

1) Thermoregulatory sweating is influenced by cutaneous temperature at temperatures in excess of 33°C.

2) The mechanism for cutaneous temperature modification of sweating is a neurally-mediated effect of cutaneous thermoreceptor activity.

3) For lower body skin temperature change, the mean sweating rate change is 0.07 $mg/cm^2 \cdot min \cdot C°$ in the five subjects studied.

4) There is approximately a three-fold variation among the individuals studied of the sensitivity of sweating rate changes to skin temperature variations.

5) Head skin temperature produces changes in measured deep head temperature including oral and tympanic membrane temperature.

6) The changes in deep head temperature produced by head skin temperature changes may be mediated by a countercurrent thermal exchange between venous blood draining the skin and arterial blood supplying the head.

7) Indirect evidence suggests that the countercurrent heat exchange which modifies tympanic membrane and oral temperature during head skin heating and cooling may also affect hypothalamic temperature.

8) The countercurrent thermal exchange in the human head may affect thermoregulatory responses to heat and cold as well as providing a selective mechanism for brain cooling during thermal stress.

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The final copies have been examined by the director of the dissertation, and the signature which appears below verifies the fact that any necessary changes have been incorporated and that the dissertation is now given final approval by the Committee with reference to content and form.

The dissertation is, therefore, accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

December 4, 1980
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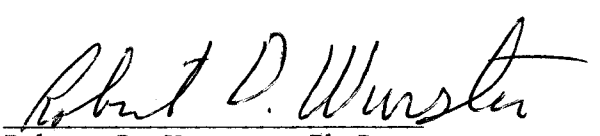
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