icism. This unique feature suggests hematopoietic tolerance. In anticipation of skin allograft studies to demonstrate immunologic tolerance between twin marmosets, skin autografts were attempted. A successful technique for fitted skin grafts to the chest emerged from the consideration of hair-growth phase, graft size and site, surgical anesthesia, control of infection, and mechanical protection. Of a series of 50 consecutive autografts reported, 48 survived.

We wish to express our thanks to Gretchen Humason for her work in preparing the histologic sections; we are indebted to and thank Ralph Hall, D. V. M., for his assistance with the electroanesthesia instrument. We also wish to thank Tom Smith, Mark Brewer, and James Kline for their technical assistance in handling and maintaining the animals.

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Sudomotor Activity as Affected by the Thermal Status of the Skin in a Warm Environment* (32824)

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Although human eccrine sweating is primarily mediated through an alteration of the intracranial temperature, an influence of skin temperature on sweating activity has been demonstrated by several investigators (1, 3, 10, 13, 14). In an earlier publication (4) from this laboratory it was concluded that the cutaneous thermal status can affect the sweat output in two ways. One of these acts through the reflex pathways involving the peripheral thermal receptors and the central nervous system and the other, a direct effect, acts locally, either on the sweat gland or on the neuroglandular junction. This latter effect is observable within the range of ambient temperatures in which sweating normally occurs; and thus is considered to be different from the direct effect noted by Randall (8) and by Issekutz *et al.* (6) where sweating was initiated at a very high skin temperature in a cooler environment.

Attempts were made to further characterize the influence of the thermal status of the skin on the rate of eccrine sweating acting by two different mechanisms. The results of these experiments are reported herein.

Methods. The experiments were carried out on 6 healthy male subjects, 20–33 years old at different ambient temperatures. Cutaneous

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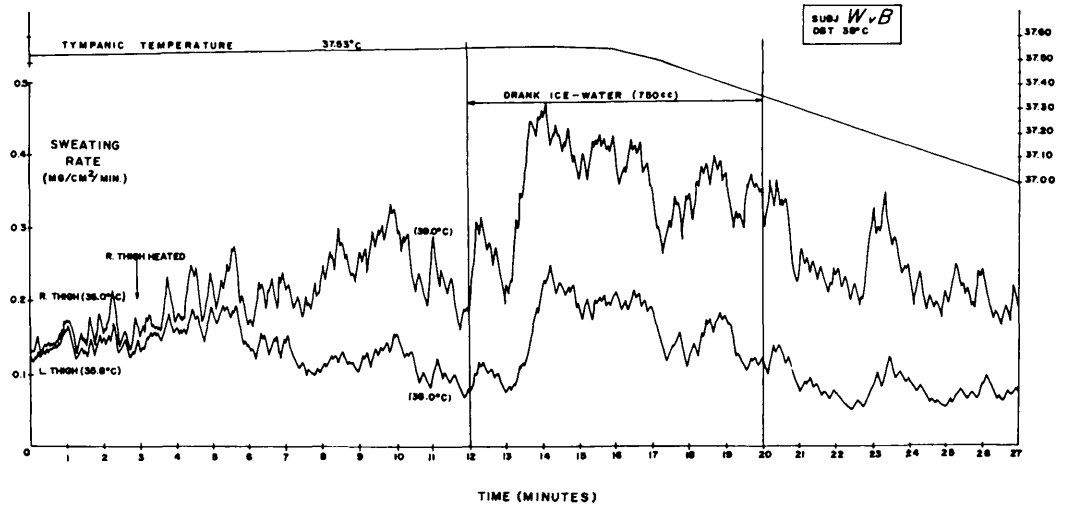

FIG. 1. The effect of drinking ice water on tympanic membrane temperature and sweating rates in the thighs (at an ambient temperature of 38°C). The temperature of the right thigh was maintained at 39°C throughout the experiment.

water loss was measured from three small skin areas of 12 cm^2 each by the resistance hygrometry method (15). In this method air of preset relative humidity is passed over the selected area of skin and changes in humidity in the efferent air are continuously recorded. Rectal temperature was determined by means of a YSI, 401 probe and for the measurement of the tympanic membrane temperature a thin flexible probe with a small (VECO 32A8) thermistor bead was used. Sweating rates and the internal temperatures were recorded continuously on a Honeywell 1108 Visicorder system. A continuous record of temperatures under the capsules covering the thermally altered skin areas was also obtained by means of thermistors and the Visicorder. Temperatures of different uncovered skin areas were recorded every 32 sec on a 16-point Brown recorder with 24-gauge copper constantan thermocouples.

Three different experimental approaches were made. The experimental manipulations of altering the temperature of a skin area and of arterial occlusion involved in the first and the third group of experiments have been previously described (4). In the second group of experiments, two subjects equilibrated at controlled environmental temperatures initially breathed from outside the climatic chamber through a low-resistanace modified Otis-McKerrow respiratory valve (Warren E. Collins, Inc.). Without any notice, the subjects inhaled 7% carbon dioxide for 4-min periods at 30-min intervals. Prior to carbon dioxide inhalation the skin temperature under one capsule was artificially maintained at a selected temperature.

Results. (1) Local influence of the skin temperature as affected by internal temperature changes. The local influence of skin temperature on sweating was observed in the presence of the influence of central temperature in the opposite direction. The experimental design of Benzinger (2) with the subject ingesting sherbet was utilized with slight modifications and the results are shown in Fig. 1. The subject was allowed to reach a thermal equilibrium in an environmental chamber maintained at 38.0°C. One sweat capsule was placed on each thigh. The temperature of the skin recorded under each capsule was 36.0°C. The temperature of the right thigh was artifically raised to 39.0°C. This procedure resulted in a higher sweat secretion on the heated area as compared to that of the nonheated area. The subject drank 750 ml of slushed ice water in a period of 8 min. The tympanic membrane temperature dropped from 37.5 to 37.0°C and a marked decrease occurred in the sweating rates as recorded from the thighs. These resulting

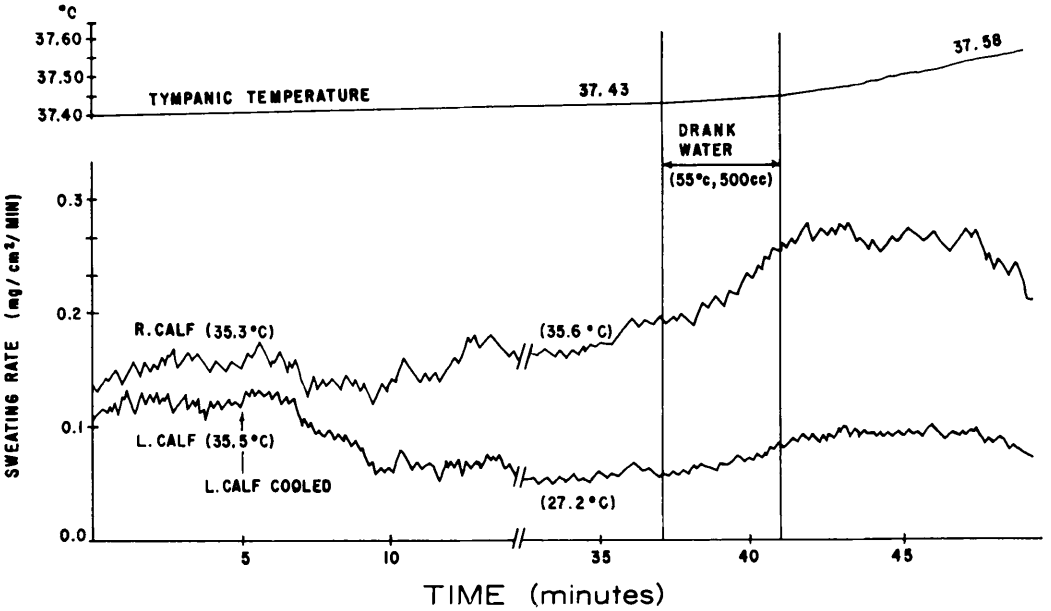

FIG. 2. The effect of drinking hot water on tympanic temperature and sweating rates in the right and left calves. The temperature of the left calf was maintained at a temperature of 27.2°C.

thermal changes were similar to those obtained by Benzinger (2) and by Stolwijk and Hardy (12). However, the effects on the sweating levels in the two thighs following the decline of central temperature were not identical, but were strongly influenced by the local temperature of the thigh.

A similar protocol was adopted in two other experiments on a different subject. Here, one of the contralateral skin areas was maintained at a lower temperature and the cranial temperature was raised. The latter was accomplished by drinking hot water (Fig. 2) and by arm exercise (Fig. 3). A rise in central temperature was accompanied by an increase in sweating rate of both the right and the left calves. Again, dissimilar response of the sweat glands in the two areas was due to the difference in the local skin temperature of the two calves.

(2) Local skin temperature and sweating induced by carbon dioxide inhalation. Inhalation of carbon dioxide by the subject equilibrated at 38.0°C proved to be an effective stimulus for sweating in the three different skin areas tested (Fig. 4). The magnitude of the sweating response was directly related to local skin temperature. In the first two periods, the right thigh with a higher local temperature had a higher sweating rate than that of the left which was maintained at a lower skin temperature. During the third period, the skin temperature of the left thigh was raised above the temperature of the right thigh. Consequently the left thigh yielded a higher sweating rate than of the right thigh.

The integrated rates of sweating during both a 5-min control period and in the last 3 min of a 5-min carbon dioxide inhalation period were determined for the thermally altered area in another subject. In order to correct for cyclic variation in sweating rate the results were expressed as a ratio of the mean sweating rate of the thermally altered region to the simultaneous mean sweating rate of a contralateral area (Fig. 5). The areas used were located on the lateral aspect of the left and right thighs. The slope of the plot of the response versus temperature was nonlinear; the Q_{10} between 22.0 and 33.0°C approximately 3.0 and that between 33.0 and 40.0°C was 4.0–5.0. No attempts were made to determine values above a skin temperature of 40.0°C as it is beyond the usual physiological range of skin temperature. Similar Q_{10}

values between local skin temperatures and the sweating rates were obtained earlier at different body temperatures when the only stimulus for sweating was the alteration of temperature of the skin area (4).

(3) Local influence as affected by the

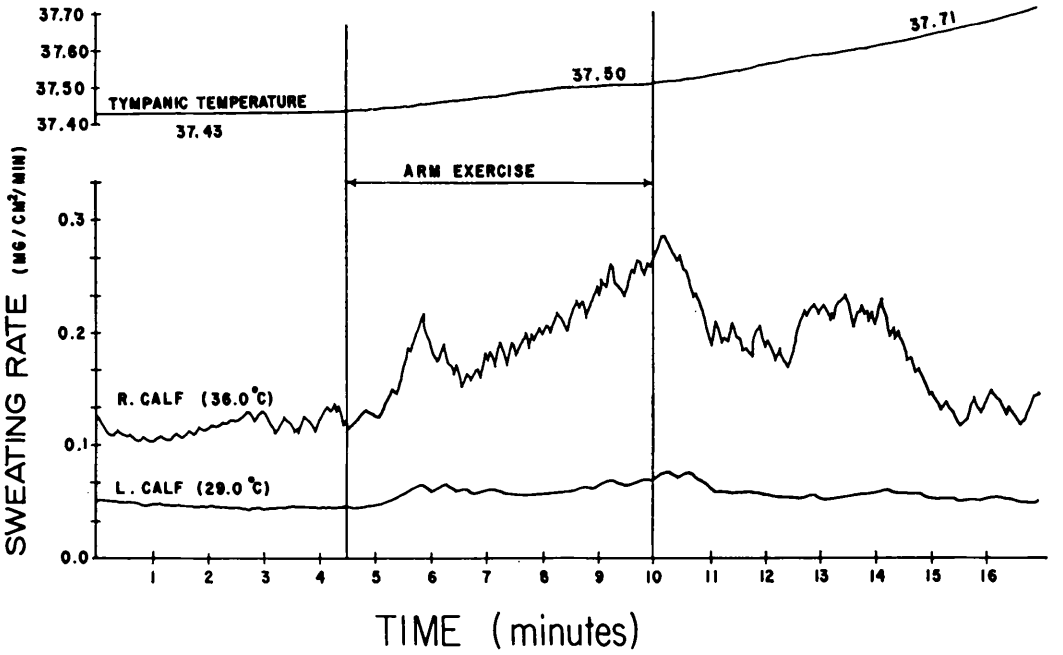

FIG. 3. The effect of arm exercise on tympanic temperature and sweating rates in the calves. The left calf skin temperature was maintained at 29.0°C.

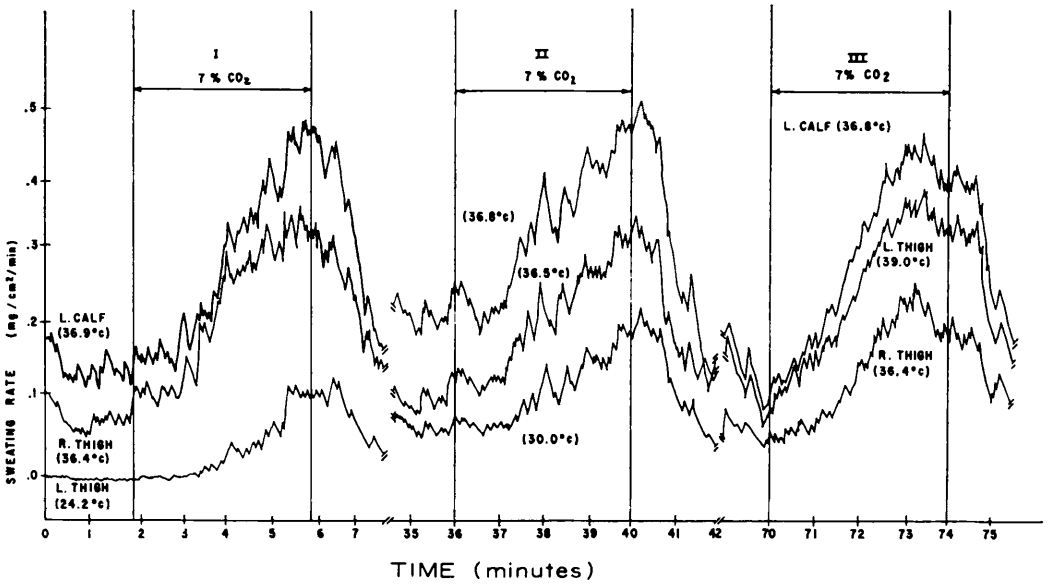

FIG. 4. The effect of inhalation of carbon dioxide on sweating rates in three different skin areas. During the first two period the temperature of the left thigh was maintained at a lower level than that of the right thigh. During the third period the relative temperature levels of the two thighs were reversed.

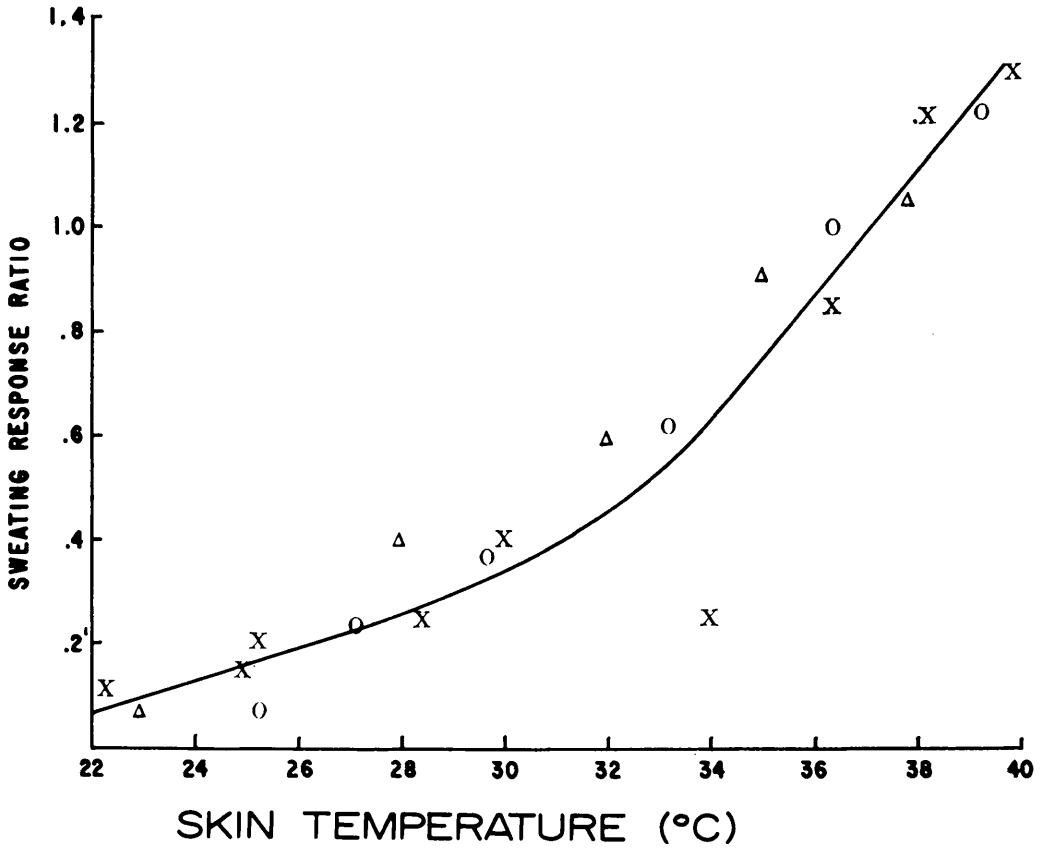

FIG. 5. The influence of skin temperature on sweating induced by inhalation of CO_2. The abscissa represents the temperature of the thermally altered skin area. The ordinate represents the ratio of the sweating rate of the area to the sweating rate of the contralateral skin area (at each skin temperature).

reflex stimulation of the sweat glands. The response of the sweat glands to cutaneous temperature changes involving the reflex pathways was also seen to depend on the local temperature of the skin area (Figs. 6 and 7). A pneumatic cuff was inflated to supra-arterial pressure for 15 min on the right upper arm of two subjects equilibrated at a room temperature of 36.0°C. The skin temperature under the capsule of the left thigh was maintained at 38.0°C while the right thigh recorded a temperature of 35.0°C. During the period of arterial occlusion, the sweating level on the two thighs following the reflex increase caused by the exposure of the right forearm to an infrared lamp was not identical but depended on the local skin temperature of the area (Fig. 6). Similarly the two thighs maintained at different temperatures had unequal sweating rates following the reflex decrease due to the immersion of the right forearm in a cold water bath (Fig. 7). Besides, the recovery in the sweating activity after the depression associated with the release of occlusion was earlier on the left thigh which had a higher skin temperature.

Like the local effect, the reflex response was found to depend upon the overall thermal status of the subject. Water-bath experiments for reflex stimulation of the sweat glands were conducted at two different room temperatures, viz. 35.5 and 38.0°C. Here, the right upper thigh was occluded and the right lower leg was immersed for 5 min in water baths maintained at different temperatures. The peak response in sweating rate of the left forearm following the leg immersion was plotted against each bath temperature (Fig.

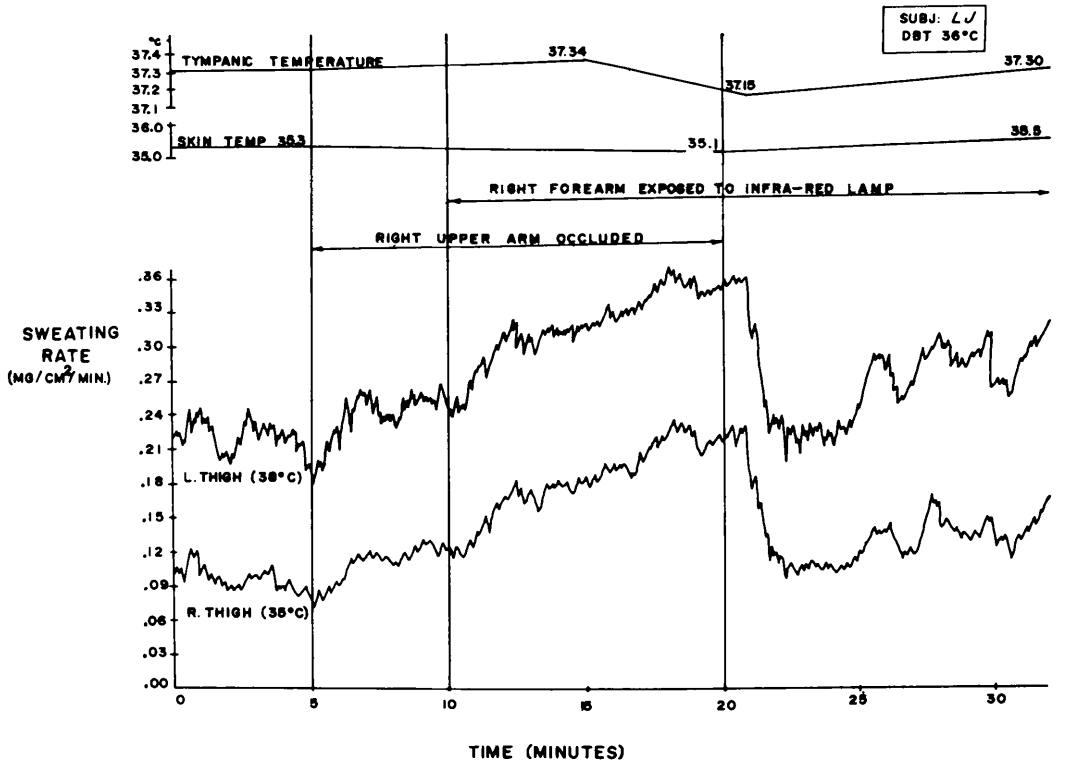

FIG. 6. The effect of infrared heating of occluded arm on sweating in remote areas. The left thigh was maintained at a higher skin temperature than that of the right thigh.

8). The graphs show that the sweating rate in the arm was directly related to the temperature of the bath. With an increase in bath temperature, there was a lesser depression in sweating activity. In addition, at the same bath temperature, the depression was less with higher room temperature. Either a higher hypothalamic temperature or an increased surface temperature at 38.0°C raised the sensitivity of the sudomotor system to the thermal stimulation of the peripheral receptors.

Discussion. It is obvious from the results reported here that the local influence of skin temperature on sweat gland function is a consistent one. The influence is exerted both below and above the skin temperature level of 33°C. The latter observation is in disagreement with the conclusion reached by Benzinger (2), who maintains that no thermal information from the body surface is sensed by the brain when the skin temperature is above 33.0°C. In Fig. 1, the difference in sweating rates in the two thighs, one at a skin temperature of 36.0°C and the other at 39.0°C with a steady tympanic temperature of 37.5°C cannot be explained by Benzinger's hypothesis. This is also true in the case of other experiments (Figs. 6 and 7) where two contralateral skin areas, one at 35.0°C and the other at 38.0°C skin temperatures had different sweating rates under a uniform tympanic temperature. These skin temperatures are within the normal physiological range and thus are not subject to the criticism rendered to the experiments of Randall (8), where the pain factor may have been involved.

Utilizing the much discussed experimental design of Benzinger (2) with some modifications, the local influence of skin temperature on sweating activity in that area has also been demonstrated in the presence of a changing internal temperature (Figs. 1–3). In spite of the strong influence of a rising or a decreasing cranial temperature on the activity of the sweat glands, the magnitude of the response

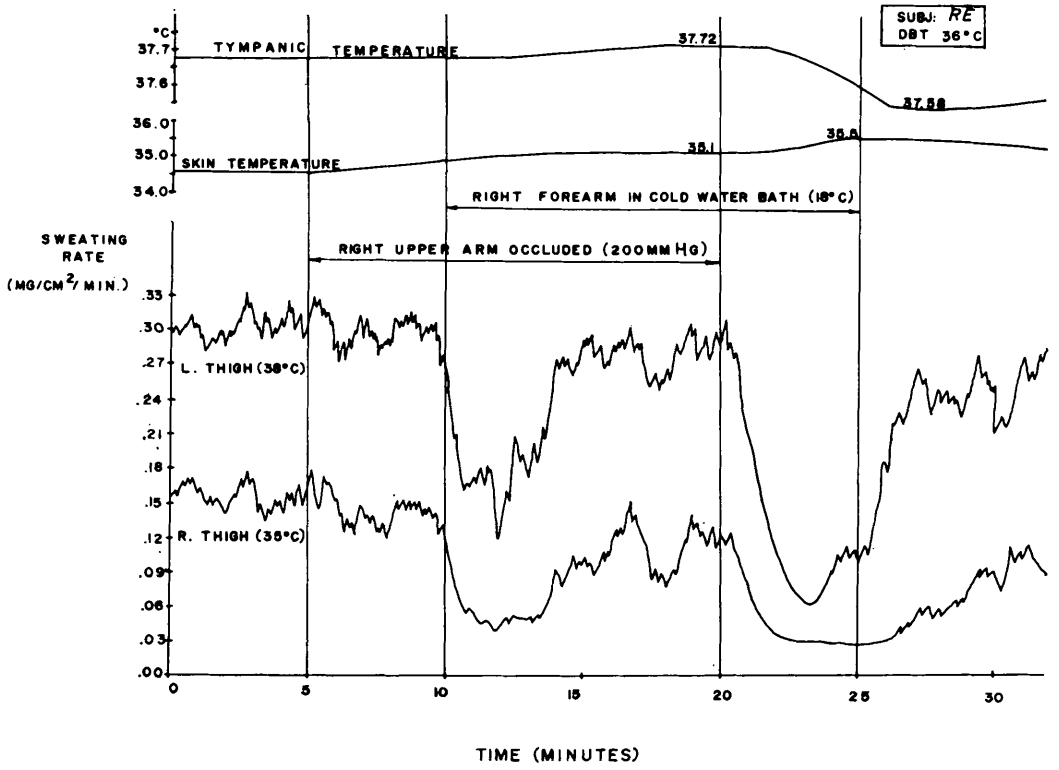

FIG. 7. The effect of cold water immersion of occluded arm on sweating in remote areas. The left thigh had a higher skin temperature than the right thigh.

by the glands was found to be directly related to the local temperature of the skin.

It was also observed that the response of the sweat glands stimulated centrally either by an elevated body temperature or by inhalation of carbon dioxide was modified peripherally by the temperature of the surrounding skin areas. A similar response of the glands was also reported when muscular exercise as a potent nonthermal stimulus for generalized sweating was utilized (14). With carbon dioxide inhalation, the Q_{10} value obtained for sweating was 3 below 33.0°C and the quotient changed to 5 above this temperature. Thus the physical processes of diffusion and aqueous vapor tension do not seem to be the contributing factors in the local influence of skin temperature observed.

The independent effect of skin temperature acting locally on the sweat glands has also been demonstrated in the presence of other influences of skin temperature involving the reflex pathways (Figs. 6 and 7). Thus it is apparent that the influence of skin temperature on the sweat glands is exerted both locally and also through the sweat centers. The clear evidence for the participitation of thermal receptors in reflex sweating was first presented by Randall *et al.* (9).

Like the direct effect of a very high skin temperature on the sweat glands reported by Randall (8) the local influence observed in our experiments was also extremely localized, thus eliminating any kind of reflex, neural involvement. However, in order to demonstrate this response a functional neural activation of the sweat glands appeared essential. Heating a skin area within physiological temperature range when the sweating center was not in an active state, did not result in localized sweating. It is safe to assume that such a functional state of the sudomotor system was not existing in the experiments of Randall (8) which were conducted at lower environmental temperatures where excessive heat application was necessary for the initiation of

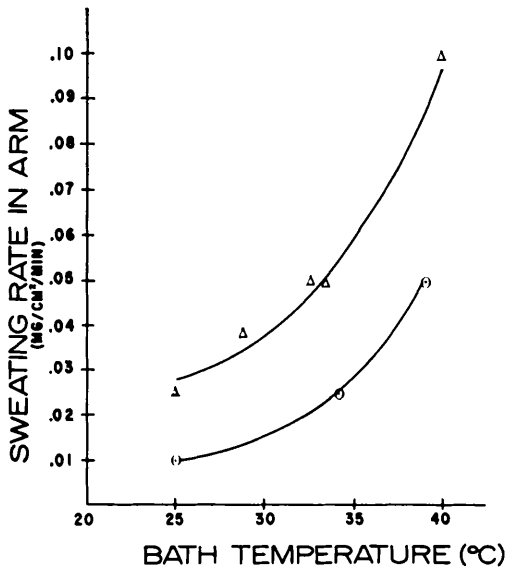

FIG. 8. Effects on the sweating rate in the arm due to immersion of an occluded leg in water baths of various temperatures at ambient temperatures of 38.0°C (upper curve) and 35.5°C (lower curve).

sweating. Denervated sweat glands in patients with unilateral lumbar sympathectomy were also found by Janowitz and Grossman (7) to respond with localized sweating accompanied by erythema and blistering when their skin was exposed to intense radiant heat. Issekutz *et al.* (6) encountered greater difficulty in eliciting abundant local sweating by intense local heating at ambient temperatures of 18–20°C than at 29–30°C.

It is thus evident that the hypothalamic center exerts the primary control action on the sudomotor system. However, enough experimental evidence has been presented to indicate that the central action is modified peripherally depending on the temperature of the body surface. Further, our results also suggest that the interaction of the peripheral influence on the neural impulses arriving at the sweat glands is multiplicative in nature. In the absence of neural drives to the sweat glands, raising the skin temperature to physiological maximum did not produce sweating. Similarly in a series of experiments with three subjects, it was found that a minimum surface temperature was also necessary to elicit a sweating response. Nonsteady state experiments were conducted to raise the cranial temperature of the subjects by drinking 750 ml of 55°C water in 10 min. The minimum ambient temperature at which the above procedure elicited sweating was 26.0°C and the corresponding mean weighted skin temperature of the subject was 32.3°C. On the other hand the similar procedure failed to produce sweating at an ambient temperature of 24.0°C and a mean weighted skin temperature of 31.3°C, in spite of the fact that the tympanic temperature increased from 36.90 to 37.15°C due to the drinking of the hot water. The active group of workers in this field at the John B. Pierce Foundation Laboratory (13) have described the thermoregulatory system by a proportional control model with two set points, one for the hypothalamic temperature and the other for the skin temperature. In their latest publication, Hardy and Stolwijk (5) observed that the evaporative heat loss of their resting subjects during the thermal transient and the steady state could be appropriately described by the product, 70 $(T_{\text{tympanic}}-^{36.6}) \times (T_{\text{skin}}-^{35.5})$, both the terms being positive. In analog simulation of thermoregulatory responses a multiplier rather than a summer has been used to simulate the interaction between the hypothalamic and the skin temperature (11, 12).

Summary. With experiments conducted in a warm environment it has been shown that the temperature of the skin exerts a consistent influence on the sweating activity in man. Skin temperature, both below and above 33°C acts locally on the sweat glands. In addition, it also acts through the reflex neural pathways. The local effect could be demonstrated even when the driving force of the internal temperature was in the opposite direction. The peripheral influence of skin temperature on sweat glands was present when the glands were stimulated by carbon dioxide inhalation. The local effect of skin temperature did not appear to involve any reflex arc; nor could it be ascribed to changes in physical phenomena like diffusion and aqueous vapor tension on the skin surface. The interaction of intracranial and cutaneous temperatures on sudomotor activity appeared to be multiplicative in nature.

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Sulfate Metabolism in the Intestinal Mucosa of Weanling and Adult Rats* (32825)

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The sulfate radical is physiologically and pharmacologically important to a variety of biological processes since it participates in the metabolism of many endogenous and exogenous substrates (1–3). Primarily, hydrolyzing (sulfatase) and transferring (sulfokinase) enzymes are involved. Studies which characterize these enzyme systems have been pursued principally in mammalian liver. However, sulfate metabolism also has been demonstrated in several other tissues, including the mucosa of the intestine of adult rats (4,5). This would permit orally administered compounds to undergo biotransformations involving sulfation or desulfation in the gastrointestinal tract. Such metabolic activity conceivably may play a very important role in detoxication and/or absorption processes involving facilitated or active transport.

The activities of several enzymes present in the mucosa of the intestine, their activity patterns during development, and their relationship to physiological events have been reported (6–8). Preliminary investigations in our laboratories demonstrated a difference in sulfate metabolism of immature vs adult rats. Peak activity in the intestine appeared to occur at 13 days of age with a progressive decline to adult values. The present study represents a further investigation of this phenomenon and an attempt to delineate the respective roles of sulfokinase and sulfatase enzymes in jejunal and ileal portions of the small intestine at two stages of development. Direct comparisons have been drawn between intestinal enzymic activity in suckling (13-day-old) and adult (43-day-old) rats.

Materials and Methods. Thirteen- and 43-day-old male and female albino Wistar rats were employed as experimental animals. Thirteen-day-old rats were suckled by their mothers and adults were maintained on regular Purina Lab Chow and water *ad libitum*. The animals were sacrificed by decapitation, the

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[1] On leave of absence from the Institute of Mother and Child Care, Prague, Czechoslovakia.