

fection was labeled with iodine-125 (9). This labeled eluate was incubated with antisera to K, L, and IgM. Each of these three antisera precipitated 90 to 95 percent of the labeled IgM. These experiments suggest that cold agglutinins obtained from patients with *M. pneumoniae* infections contain K and L determinants in the same molecule (10).

Cold agglutinins exclusively of L type have not yet been found. It is, therefore, possible that, in cold agglutinins containing both types of light chains, cold reactivity depends upon the presence of the type K chain. The consistency of the finding of cold agglutinins of the K type in the 59 patients with chronic cold-agglutinin disease which have been reported (5), and in our patients, favors the hypothesis that these monotypic antibodies may be the product of single clones of malignant cells.

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10. The finding of two different light-chain types in the same cold agglutinin molecule is in apparent contradiction to the immunodiffusion pattern of nonidentity (Fig. 1G). The contradiction is best explained by the heterogeneity of the molecules in the antigen well. IgM is a polymer, probably a pentamer of 7S subunits which contain two heavy and two light chains [F. Miller and M. Metzger, *J. Biol. Chem.* **240**, 4740 (1965)]. The ratio of K to L chains in these molecules may vary and thus produce immunodiffusion patterns of nonidentity. Similar observations have been made by W. E. Paul and B. Benaceraf, *J. Immunol.* **95**, 1079 (1965), and also discussed by A. J. Crowle, *Immunodiffusion* (Academic Press, New York, 1961), pp. 75-77.
11. We thank Dr. J. P. Griffin from the U.S. Great Lakes Naval Hospital, Great Lakes, Ill., for supplying the sera of patients with *M. pneumoniae*; Dr. Lee from the Mount Sinai Hospital, Chicago, Ill., for the sera of patients with infectious mononucleosis; and L. Hall for technical assistance.

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## Sweating Exercise Stimulation during Circulatory Arrest

**Abstract.** We have direct evidence of neurogenic stimulation of human exocrine sweating by muscular exercise. Sweating was markedly increased when warmed venous blood was prevented from reaching the heat-loss center in the hypothalamus.

There is an augmentation of sweating within 1.5 to 2 seconds after the initiation of heavy muscular work by human subjects in a warm environment (1). The stimulus for this increase of sweating during the first few seconds of work appeared to be non-thermal, as warmed blood from the working muscles could not have reached the centers which regulate heat dissipation. From this observation we concluded indirectly that certain sweating responses during exercise in a warm environment can be independent of changes in central temperature.

Direct evidence of neurogenic stimulation of the sweating mechanism during muscular exercise has now been obtained from experiments in which the return of warmed venous blood to the heat-loss centers was prevented by arterial occlusion. Three healthy young adult male subjects performed isometric contractions against a stiff elastic cord while the circulation to and from the working muscles was arrested by an inflated pneumatic cuff which was placed high around the upper arm. With the elbow remaining on the

arm rest of a chair, the flexor group of the arm musculature was contracted, the forearm being raised approximately 30° above its resting position. The subjects made no additional movements during the arm-muscle contractions, which lasted 75 seconds (Fig. 1) and 120 seconds (Fig. 2) in different experiments. The sweating rates were continuously and simultaneously recorded from small skin areas of nonoccluded limbs by the method of resistance hygrometry (2).

Figure 1, B and D, shows that, while venous blood warmed by the working muscles could not activate the heat-loss center in the hypothalamus for at least 75 seconds, the rate of sweating increased 3 to 4 times above the sweating rate during rest. Some participation of pain fibers during the ischemic muscular contractions cannot be ruled out. However, the perception of pain was not apparent during the first 35 or 40 seconds, when the rates of sweating had increased 2.5 to 3 times over the resting values.

It has been suggested that thermoreceptors in the muscles, or in the veins

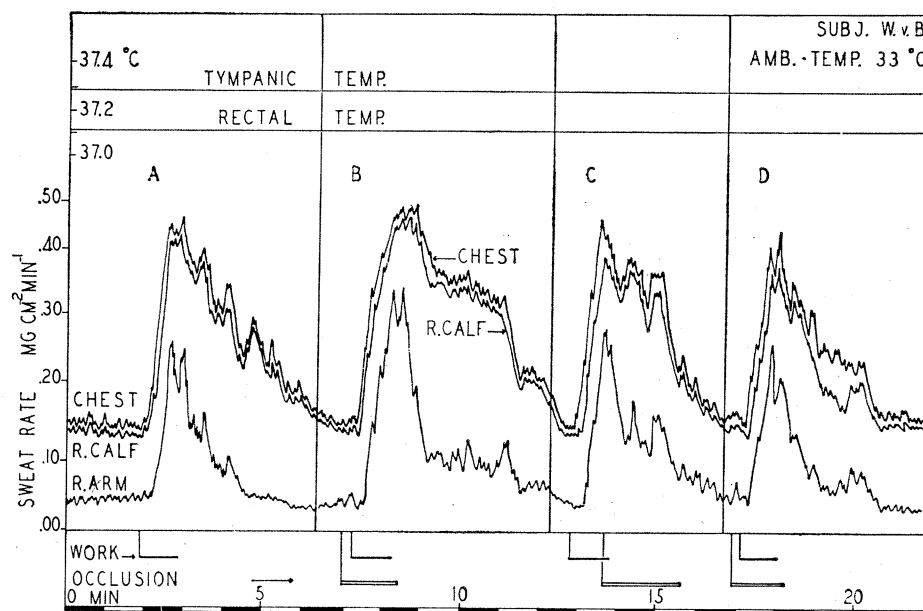


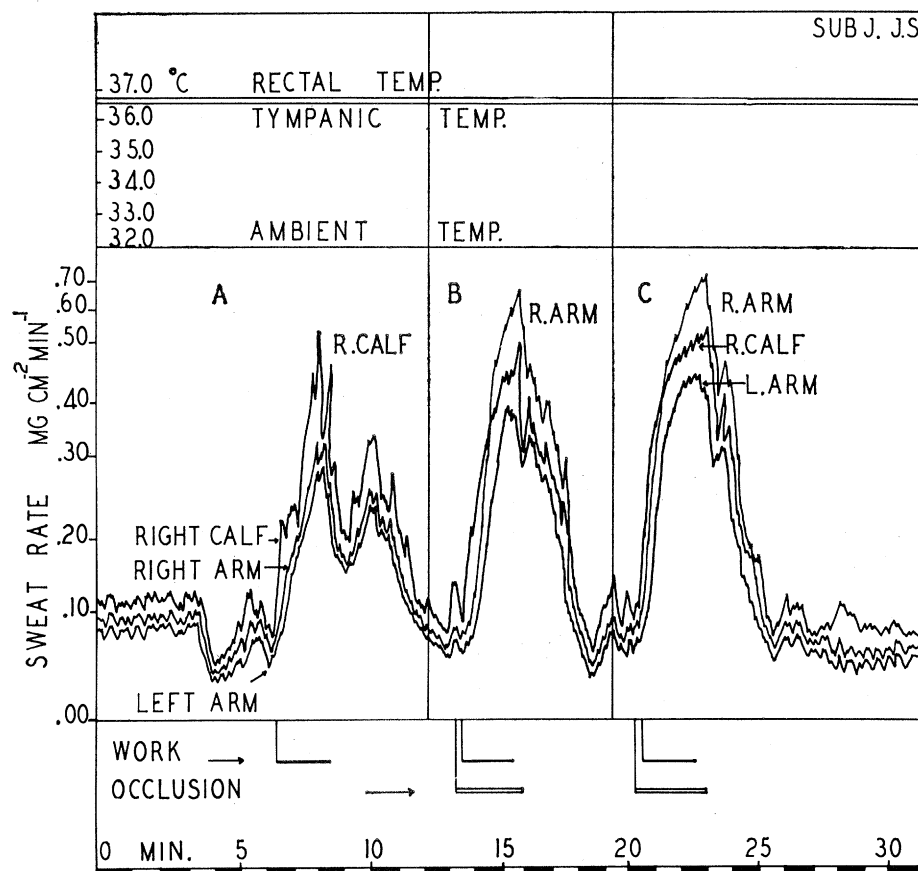
Fig. 1. Continuous recordings of sweating from three different skin areas during isometric exercise with the left arm. Experiment A: no occlusion. Experiments B and D: occlusion on left arm during contraction. Experiment C: occlusion on left arm after muscular exercise. Work, isometric contractions; occlusion, 200 mm-Hg.

Fig. 2 (right). Continuous recordings of sweating from three different skin areas during 2 minutes of work at 32°C dry bulb, 30 percent relative humidity, on a bicycle ergometer. In experiments *B* and *C* the left upper arm was occluded 30 seconds before initiation of the exercise. Work, 750 kg/min; occlusion, 200 mm-Hg.

draining warm blood from the active muscles, could participate in the sweating responses during exercise (3). This hypothesis was tested by experiments in which the pressure cuff was inflated 5 seconds before the cessation of the muscular contractions, so that no stimulation of pain receptors would interfere with the sweating responses after the work (Fig. 1*C*). Even though no warm blood could escape from the exercised muscles and their venous drainage, an immediate decrease of sweating was observed after the cessation of the contractions. The results of these experiments indicate that the afferent drives for the increased sweat secretion during muscular work are at least partially of a neural nature.

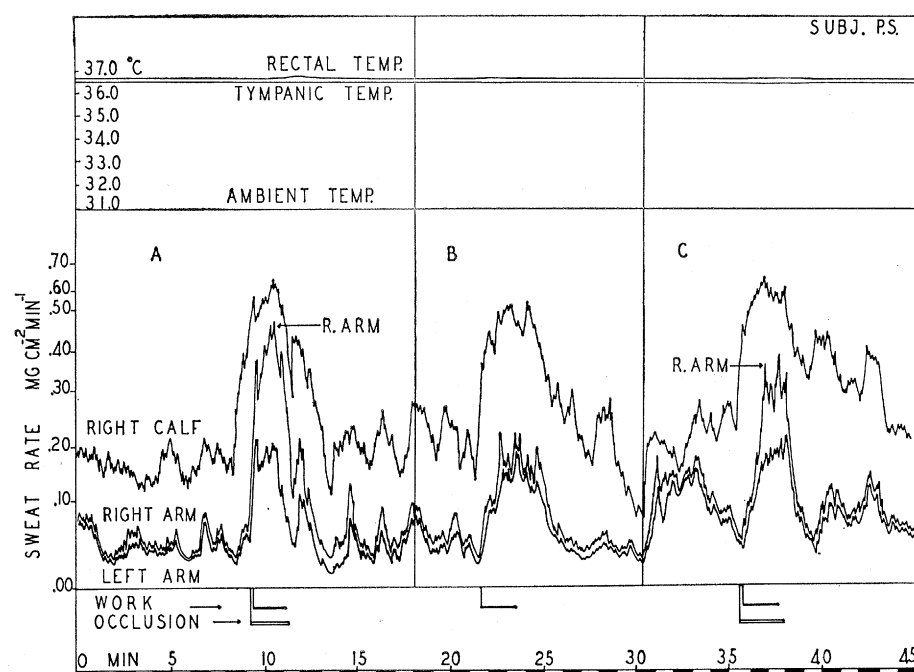
The effect of arterial occlusion on the immediate responses at the initiation of muscular work was also evaluated in experiments in which the blood supply to a nonworking limb was obstructed. The sweating rates of three resting subjects were augmented two to five times within 2 minutes by physical exercise consisting of pedaling a bicycle ergometer at a work rate of 750 kg-meters per minute. The left arm was occluded 30 seconds before the start of the work, and the sweating responses of this arm were compared with responses of the same arm during exercise without occlusion (Figs. 2*A* and 3*B*) and with sweat rates simultaneously recorded on the contralateral arm and lower leg. Figures 2 (*B* and *C*) and 3 (*A* and *C*) demonstrate that an immediate moderate or great increase in sweat excretion could be evoked on the left

Fig. 3 (right). Continuous recordings of sweating from three different areas of skin during 2 minutes of work at 31°C dry bulb, 30 percent relative humidity, on a bicycle ergometer. Note the similar responses of the left forearm during and without occlusion and the instantaneous higher responses of the contralateral forearm during occlusion of the left arm. Work, 750 kg/min.



arm, in spite of the fact that the circulation to the limb was arrested. While these results suggest that the effector side of the stimulation of sweating by exercise is strictly neural, it has been found that 4 minutes of circulatory arrest before exercise re-

duces the immediate sweating responses of the occluded arm by about 50 percent. Because rapid and large variations in sweating can be observed during arterial occlusion, it seems doubtful that the sweating responses during exercise are dependent on higher



concentrations of adrenalin or other humoral agents in the circulating blood (4).

Excessive increments in sweating were recorded on the nonoccluded limbs, particularly contralateral to the exercising limb (Fig. 3). Kuno (5), Randall *et al.* (6), and Collins *et al.* (7) have described similar observations of increased sweating at rest of the arm contralateral to the occlusion. However, our results suggest that the development of the high contralateral sweating responses is much faster in exercise than during rest. The mechanism is unexplained, but the possibility of mediation through cutaneous pressure or vascular baroreceptors, or both, must be considered.

The immediate responses of the sweat glands to stimulation by exercise indicate that the afferent side of the impulse-conduction system is dependent on a neural sensing mechanism. Our earlier data did not reveal whether this sensing mechanism was activated through factors directly related to the muscular contractions or through local heat receptors. However, it is doubtful whether enough heat can be liberated within 2 seconds after the initiation of muscular work to produce the highly augmented sweat responses. The participation of local heat receptors in muscles or veins (3) seems unlikely, since prevention of heat removal by circulatory occlusion did not abolish the sharp decrease in sweating after isometric exercise (Fig. 1C).

The demonstration by Robinson (8) that both internal and skin temperatures participate in the regulation of sweating during work is in accord with our findings. It appears that the various thermal parameters provide a setting of the heat-loss system for afferent impulses from the neuromuscular system. Our observations substantiate the opinions of Asmussen (9), Minard (10), Bradbury (11), Keller (12), and Nielsen (13) regarding the direct effect of exercise on the thermoregulatory system. Our evidence tends to refute the concept that an elevation of the hypothalamic temperature is essential for increased sweating during all physical work in a warm environment (14). One possible mechanism is suggested by Jackson and Hammel (15) who concluded after experiments on exercising dogs that there is a lowering of the thermostatic set point during exercise. The observed direct rela-

tion between the sweating responses and the work load under presumably constant thermal excitation (16) suggests that either muscle receptors or irradiation of motor impulses play a part in the increased excitation of the sweating mechanism.

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### Cutaneous Water Loss in Reptiles

In their report on water loss in reptiles [*Science* **150**, 1547 (25 March 1966)] Bentley and Schmidt-Nielsen considerably diminish the force of their conclusions by using the very crude formula of Benedict to estimate the surface areas of the animals. No account is taken of the very different shapes of the five species or of the relatively water-impermeable shells of the turtles. The principal effects of this oversimplification are (i) underestimation (relative to the caimans and lizards) of the rate of cutaneous water loss per unit surface area in the two turtle species and (ii) underestimation (relative to *Pseudemys*) of the rate of cutaneous water loss per unit surface area in *Terrapene*. Appropriate adjustments of the data

would make a strengthened case for rejecting the notion of the water-impermeability of reptilian skin, especially in the turtles, whose effective surface areas are so small. On the other hand, certain of the observed correlations with habitat will be altered, although surely not eliminated. For instance, the cutaneous water-loss rates are probably more similar for *Caiman* and *Pseudemys* and more disparate for *Terrapene* and *Iguana* than Bentley and Schmidt-Nielsen indicate.

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We are pleased that Hurlbert agrees with our case for rejecting the notion of the water impermeability of reptilian skin. We also feel that our data, which show substantial evaporative water loss from the integument of reptiles, would not be substantially strengthened by making "appropriate adjustments." Any person looking at a turtle must be struck by the difference between the hard shell and the soft skin, but, since no information is presently available on their relative permeabilities, it is unjustified to make any attempt to assess the relative roles in water loss of these two areas of the skin.

In regard to the adjustment of surface areas for the different shapes of animals, Benedict carefully reviewed the subject and concluded that attempts at determining surface areas to better than 10 or 20 percent are rather meaningless. He concluded his work with the suggestion that the same equation can be used as an approximation for the surface area for all tetrapods. Such errors as may occur, say, of a magnitude of 20 percent, are insignificant in comparison with our observed differences in water loss of several hundred percent.

We have continued our studies of water loss in reptiles, and we have included an examination of the relative permeabilities of various parts of the integument of turtles. Our main thesis, that the reptilian skin is by no means impermeable, is being amply confirmed.

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