Reflex Sweating and the Inhibition of Sweating by Prolonged Arterial Occlusion¹,²

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LTHOUGH REFLEX SWEATING responses have long been recognized, the precise nature of such responses is far from clear. Generalized body sweating may be induced by exposure of the body to environmental temperatures sufficiently high to raise the temperature of circulating blood. Autonomic centers in the brain stem, or centers in the spinal cord, are known to bring about profuse sweating when perfused with blood at high temperatures (1). We have observed that reflex sweating may also be induced by exposure of a very limited area of skin to radiant heat, and it appeared doubtful that increases in blood temperature could be responsible.

Employing a technique previously described for studying quantitative changes in the number of functional sweat glands (2, 3) this problem and the relationships of sweating and blood supply have been studied.

Measurements of sweat gland activity during normal sweating responses to high environmental temperatures show that alternating periods of high and low sweating activity occur similarly on both arms. Although such spontaneous peaks of sweating occur approximately simultaneously when measured on similar areas of both arms, they do not always occur exactly so and not always in the same intensity. These findings confirm the existence of bilateral control of normal sweating responses to high temperatures.

As radiant heat is applied to a relatively large area of one arm (10 to 20 sq. cm.) sweating first appears in the locally heated area of highest temperature. Sweating may then spread to neighboring areas of the same arm and if heat is sufficiently extreme and applied to a large area, sweating appears on the opposite arm (2, 3).

The question then arises, under what circumstances does sweating appear on areas adjacent to the heated area and on the opposite arm, and is

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there any segmental relationship to reflexly induced sweating on opposite sides of the body?

PROCEDURES AND RESULTS

In checking the distribution of reflex sweating when radiant heat was applied to one arm only, long strips of paper were simultaneously applied around the complete circumference of the 'reflex' arm at the wrist and upper arm. Since segmental distribution of spinal nerves to the skin of the arm involves relatively long and narrow areas extending longitudinally down the arm, a paper strip wrapped around the circumference of the arm covers several segmentally innervated dermatomes. Such dermatomes in the circumference of the upper arm derive innervation from spinal nerves C5, C6 and T2, while those in the wrist are innervated by C6, C7 and C8. Heat was applied to the ventral surface of the wrist of the opposite arm. Peaks of sweating were reached simultaneously on all surfaces of the circumference of both the wrist and upper arm on the reflex side and the subject often volunteered that he "felt sweating all over his body". There were consistently fewer glands participating in the peaks of sweating activity on the upper arm when compared with the wrist surfaces, and in some experiments there were times when a few glands were active on the wrist but none at all on the upper arm. There is evidence that sweating is less readily elicited on the upper arm when compared with more distal areas of the arm and hand. Sweating disappeared entirely from the upper arm and decreased markedly on the wrist of the 'reflex' arm immediately after removal of the heat stimulus from the opposite arm. Although the number of actively secreting glands steadily declined, sweating usually persisted in the heated area for a few moments after the heat was turned off.

Although all surfaces of the 'reflex' arm may participate in sweating responses to heat applied to the opposite arm, sweating is usually not as profuse on the 'reflex' side. That is, the output per gland is less and, provided the heat stimulus is not severely painful, the number of active glands is less on the 'reflex' side. It is true, however, that nearly the maximal number of glands for a given area may be activated by painful and psychic stimulation as well as by excessive heat over a large area of the body. It is suggested by Kuntz (i) that generalized sweating due to local heating is probably due to changes in blood temperature. In order to determine whether sweating responses such as those described above are actually of nervous origin or due to heating effects at the sweat centers and gland cells themselves, an arm cuff was placed around the upper arm on the 'reflex' side. This cuff was then rapidly inflated to levels above systolic pressure and radiant heat applied locally to the opposite arm. Profuse sweating in both the locally heated area and on the 'reflex' (occluded) arm occurred with the application of heat.
The necessity of heating effects at gland cells themselves was thereby ruled out.

The possibility of temperature increases at sweat centers in the brain and spinal cord remained. A cuff was therefore rapidly inflated to levels above systolic pressure around the upper arm on the heated side. Blood could thus neither enter nor leave the area warmed by radiant heat, and again sweating was widely distributed over both the locally heated area and over the opposite ('reflex') arm. With the cuff still inflated, the heat was turned off and sweating on the 'reflex' arm immediately decreased or stopped. Sweating on the heated (occluded) arm persisted longer than in the normal, non-occluded arm presumably because accumulated heat set up local sweating responses. That reflex sweating may be induced, therefore, by stimulation of peripheral receptors without participation of temperature increases at the sweat centers in the central nervous system via the circulation of 'warmed blood' is thus conclusively demonstrated.

Influence of Arterial Occlusion. Sweating has been reported in the amputated human limb following electrical stimulation of the nerves (4). That sweating may occur in the absence of circulation is thus established, but sufficient information on the duration of such responses and the results of arterial occlusion in a normally sweating extremity is lacking.

Figure 1 illustrates the sweating responses during prolonged arterial occlusion. The environmental temperature was relatively high (31° to 32°C.) and sweating was profuse throughout the control period, although a still greater number of sweat glands were reflexly stimulated into activity by application of radiant heat to the opposite arm. In order to prevent

![Diagram of sweating and skin temperature responses](image-url)
venous congestion, arterial occlusion was accomplished by rapid inflation of an arm cuff around the upper arm from a pressure reservoir. Sweating patterns remained essentially unchanged for 6 to 7 minutes after which the number of functional glands progressively declined to very low levels. It is apparent however that cyclic phases persist even though the total number of active glands is considerably decreased. After 10 minutes of depressed sweating on the occluded arm radiant heat was applied to the opposite arm in the same manner as in the control period. A low peak of sweating on the occluded arm represents a reflex sweating response of considerably lower order than that occurring during the control. The fact that relatively few glands responded to the same stimulus which had previously induced a profuse response indicates an alteration in irritability of the sweating mechanism. That the depressed irritability was confined to the ischemic area was indicated by a profuse, generalized sweating response on other body surfaces during the application of heat. It is true, however, that in some experiments peaks of sweating as high as those observed in the normal were obtained by application of heat directly to an area in which sweating was reduced during prolonged arterial occlusion. In such experiments however, the stimulus was applied to the ischemic area directly and was therefore considerably stronger than that occasioned by reflex stimulation. The possibility of responses of the sweat glands to the direct stimulating action of heat cannot be eliminated in these experiments.

During the later stages of the occlusion, all sensation and motor control in the ischemic arm was depressed. In testing sensation and movement, the subject was not aware the arm was stimulated unless he visually observed
application of the stimulus. The arm was intensely cyanotic but due to the high environmental temperature and absence of sweating was not cold.

After sweating had again decreased following reflex stimulation, the arm cuff was deflated. The arm immediately became intensely hyperemic and the skin temperature rose sharply, but sweating remained at low levels (zero for 9 minutes) for 17 minutes before cyclic responses were spontaneously reestablished.

Such experiments establish the fact that sweating does not immediately stop following arterial occlusion. Cyclic sweating continues but with decreasing numbers of glands until very low levels are attained. Even at this point many sweat glands retain secretory ability as attested by the peaks of sweating which may be attained through direct or reflex stimulation.

**DISCUSSION**

Simultaneous observations of sweat gland activity on the normal, non-occluded arm demonstrate that cyclic sweating continues at normal or slightly elevated levels throughout the period of occlusion. In other words, the central sweating mechanism continues to discharge impulses in a cyclic fashion suggesting that the site of depression is distal to the arm cuff.

The fact that the sweat glands could respond to strong reflex or to direct heat stimulation would suggest the site of depression was not primarily in...
the sweat glands themselves. It would seem possible that deprivation of oxygen is the factor responsible for depressed activity and that the nerve endings (and possibly the axons) are the site of depression. Such theoretical reasoning receives support from the recent work of Wright (5) who found that excised, anoxic mammalian nerve fibers show 90 to 100 per cent reduction of action potential within 20 minutes. Wright also showed that no change occurs in action potential or polarization in mammalian nerves (cat and rabbit) for 3 to 10 minutes following exposure to an atmosphere of nitrogen. Following this period, a simultaneous depolarization and reduction in action potential proceeds rapidly for 10 to 20 minutes. It is striking that a very similar time course in depression of sweating follows deprivation of blood supply to the intact sweating mechanism. It is of historical interest that Kendall and Luchsinger (4) observed that sweating could be elicited on the dog's and cat's paws 'for the first quarter-hour' after amputation.

The prolonged depression of sweating following return of blood to the arm upon release of the occlusion pressure was somewhat surprising and suggested that factors other than, or in addition to, anoxia may be operating in preventing sweat gland activity. Figure 2 illustrates the fact that although sweating is depressed in the occluded arm, it continues at relatively normal or somewhat elevated levels on the non-occluded arm until circulation in the occluded arm is restored. Synchronous cyclic sweating was evident on both arms until late in the occlusion period when sweating in the ischemic area was definitely depressed. At this time two voluntary, deep breaths induced a comparatively high peak on the normal side with only a delayed, low peak on the occluded side. Although absolute zero levels were not observed in sweating in the ischemic arm, gradual depression was apparent during the latter part of the experiment.

When circulation was restored the skin of the ischemic arm became intensely hyperemic and warm and a severe sensation of intense pressure developed. No such obvious changes were noticeable on the normal, control arm, but attention is particularly directed to sweating responses. Immediately following deflation of the arm cuff, sweating stopped on both arms and remained depressed for 30 minutes in spite of the fact that skin temperatures continued elevated on the experimental arm and normal on the control arm. At the end of this period, voluntary deep breathing induced low-grade sweating responses in the two arms.

Such experiments suggest the possibility that during prolonged occlusion some substance may be released by ischemic tissues which depresses sweating. When this substance is released into the general circulation, sweating in other areas of the body is depressed. It remains to be determined whether such a hypothetical substance is active centrally or directly on the peripheral sweating mechanism.
Accordingly, experiments were carried out in which an arm cuff was inflated around the upper arm on the control side 15 to 30 seconds before the occlusion on the experimental arm was released. Figure 3 illustrates such a procedure. Depression of sweating during arterial occlusion is evident on the occluded arm while sweating continues prominently on the control arm. The inhibition of sweating on the control side following release of the cuff from opposite arm, in spite of the fact that circulation was arrested, indicates that the site of depression is central to the arm cuff.

Thus following a purely local inhibitory effect with little or no generalized depressant influence during the occlusion of one arm, generalized inhibition occurs upon release of some humoral agent into the systemic circulation. The inhibitory influence may be peripheral (directly upon the post ganglionic endings and the sweat glands themselves), but that this is not necessarily true is demonstrated by experiments such as those illustrated in figure 3. This leaves the possible locus of inhibition in the CNS or at the synapsis in autonomic ganglia.

SUMMARY

Local application of radiant heat to a restricted region of one arm induces reflex sweating responses on all surfaces on the opposite arm as well as on the heated arm. Such responses are not necessarily dependent upon heating effects in the central nervous system or the sweat glands themselves as indicated by persistence of reflex sweating in spite of occlusion of the blood flow from the heated arm.

During arterial occlusion, sweating may continue relatively unchanged for the first 5 to 15 minutes. Following this period there is a progressive decline in the number of functional sweat glands although cyclic phases of sweating continue until low levels of sweating are attained. Simultaneous observations on the opposite, 'control' arm during the period of occlusion show normal cyclic sweating, usually at a somewhat elevated level. Immediately upon release of the occlusion, the ischemic arm becomes hyperemic and warm, with no noticeable change in temperature on the control arm, but sweating on both arms is markedly inhibited. Such inhibition occurs on the 'control' arm even though the circulation is clamped off immediately prior to the release of the occlusion. An unknown humoral agent produced by ischemic tissues and acting centrally to depress sweating therefore is indicated.

REFERENCES

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