

Adrenergic Focal Sweating

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A report of the preliminary observations on the focal sweating induced by intradermal infiltration of epinephrine hydrochloride (Adrenalin) solution in the normal skin of 25 natives of India, acclimatized to tropical climate is presented along with relevant notes on vasomotor and pilomotor reactions. In contrast to the observations earlier reported by some other workers, the results showed complete anhidrosis in the central blanched area. Possible mechanisms of human adrenergic sweating has been reported.

THE FUNCTIONING of the sweat apparatus is of special interest to both physiologists and dermatologists as it pertains to temperature regulation, acclimatization, water and electrolyte balance, nutrition and metabolism, and to the functions of the vegetative nervous system.¹ In fact, the application of human sweat study ranges from the selection of astronauts for their ability to withstand thermal stress to the diagnosis of cystic fibrosis and other disorders, besides a large number of dermatological ailments.² Study of sudomotor functions using thermal or chemical stimuli³ and their pharmacological significance have long been recognized.⁴

Sweating has been regarded as a cholinergic (ie, parasympathetic) function since the demonstration of Dale and Feldberg.⁵ Recently, several publications have appeared presenting evidence that human sweat glands are sensitive to the action of epinephrine and related amines,⁶ question has been raised of the existence of an adrenergic component (ie, sympathetic) in the nervous mechanism of human sweat glands.⁷⁻¹² Epinephrine, norepinephrine (Levarterenol) and phenylephrine (Neo-Synephrine) induced sweating when injected intradermally

along with local vasoconstriction. This effect cannot be elicited following local injection of adrenergic blocking agents such as dibenamine (dibenzylbetachlorethylamine hydrochloride) or following sympathetic denervation.¹³ While adrenergic focal sweating has been found to be potentiated by local infiltration of acetylcholine,¹⁴ it cannot, however, be blocked by anticholinergic drugs, such as atropine.¹⁵ The spontaneous sweating induced by thermal stress, exercise, or emotion can be blocked by local infiltration of cholinergic blocking agents while adrenergic blocking agents fail to elicit any such action.^{12,16} All these observations tend to suggest the existence of an adrenergic as well as a cholinergic innervation of the human sweat glands, although its significance still remains a matter of conjecture.

As the adrenergic sweating has not previously been studied in the skin of native Indians, the present study was undertaken to obtain some information regarding the nature of the cutaneous reaction to the intradermal injection of epinephrine hydrochloride solution.

Materials and Methods

The experiments were performed on 7 female and 18 male subjects. All the subjects were healthy normal persons free from any skin or systemic disorders. The average age was 28 years (range, 13 to 41 years), 5 of the subjects were below 20 years, 11 were between 21 and 30 years, 8 were between 31 and 40 years, and only one was above the age of 40 years. The average weight of the subjects was 60 kg (range, 52 to 72 kg) and the average height was 159 cm (range, 153 to 169 cm). The observations were made usually in the morning (9 to 11 AM) and the tests were repeated thrice in each subject at an interval of two weeks.

The tests involved induction of sweating by infiltrating intradermally 0.1 to 0.2 ml of epinephrine hydrochloride solution in a dilution of

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1:10 to 1:100, the solutions having been prepared fresh with isotonic saline each time for the individual experiment. The control study was done by similarly injecting an equal amount of normal saline in an identical skin area on the contralateral side. The upper part of the forearms and medial side of the thighs were selected for the tests. The test areas were infiltrated with a 26-gauge needle fitted to a tuberculin syringe with all aseptic precautions. All the tests were performed in a room the temperature of which was maintained between 22 C to 25 C with relative humidity adjusted to 40% to 60%. The subjects were kept in that environment for about 30 minutes before the tests were performed in order to become adjusted to the prevalent conditions as well as to establish a base line for the skin responses.

The sweat response was studied by Randall's iodine-starch paper technique¹⁷ as modified by Papa.¹⁸ The basis of the technique was similar to the visual methods introduced by Minor¹⁹ and Wada.¹⁰ Papa's procedural modification avoided the use of any alcoholic iodine solution, the frequent application of which on the skin appeared irritating in many cases and which provoked anhidrosis. The method adopted consisted of the application of a suspension of corn starch and castor oil in the ratio of 9:10 over the test area with a paint brush, immediately following the intradermal injection of the stimulating chemical. The appearance of milky white droplets, conspicuously seen on the dark skin of the subjects, indicated sweating. Non-embossed paper toweling was then smoothed over the site and was gently peeled off. The starch pattern, thus transferred was immediately exposed to iodine vapor, produced by warming the elemental iodine crystals in their container in moderately warm water. Characteristic blue-black puncta developed at the sweat points. The imprints thus obtained on the paper were allowed to dry in a room without air current and subsequently were photographed for permanent recording. Repeated prints were taken from a particular site following stimulation at an interval of three to five minutes by holding the paper for 10 to 30 seconds.

Local skin surface temperature was recorded every minute from the blanched areas and control sites by a copper-constantan thermocouple connected to a null-reading Wheatstone bridge (Elektrolaboratariet Potentiometer) which can measure a temperature change of 0.1 C.

Left, Black dots represent sweating induced by intradermal injection of 0.1 cc of epinephrine hydrochloride solution. The small central zone devoid of sweating response as detected by Papa's method is commensurate with the blanched area. The dilution is 1:100. Right, The dilution is 1:10.

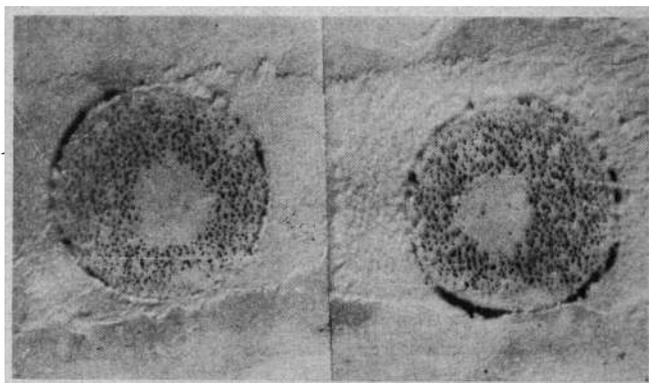
Results

The area injected with epinephrine hydrochloride solution showed immediate pilomotor reaction along with marked vasoconstriction as evidenced by blanching which was associated with lowering of skin temperature by 1 C to 2 C. The sweat dots appeared within one-half to two minutes over an area of a few centimeters (1 to 2 cm) surrounding the central blanched area. Out of 25 subjects three showed no sweat response, two others only a questionable response, and the remainder manifested the typical response as described. Irrespective of sweat response all the subjects showed positive pilomotor reaction and blanching. Sweat prints were taken up to two hours during which the blanching was seen to disappear gradually. The ability of epinephrine to induce sweating varied with the concentration but generally the onset, the duration of the response and the degree of sweating reaction were found to be more or less reproducible on different occasions; at times, however, an individual might fail to respond to a dose larger than that ordinarily effective. No apparent differences in sensitivity were observed between the sexes or among the different age groups under experimentation. In control areas neither of the reactions could be observed in any of the subjects excepting a very transient appearance of only 5 to 10 drops of sweat in some.

Curiously enough the blanched areas surrounding the point of injection remained altogether devoid of any sweating in all patients for a period of one to two hours following the local injection (the Figure).

Comment

From the foregoing data it appears that sweating can be induced by epinephrine in



human skin but not uniformly in all cases. Positive sweat reactions in 80% of the subjects tested are in close agreement with the observations of others.^{9,20} No explanation for the lack of adrenergic sweat response in about 20% of the subjects is met with in the literature. The data collected from the present study regarding the initiation, duration, and intensity of the sweating as induced by intradermal epinephrine injection corroborated the reports of other workers. In agreement with the observations of the different workers in the field the effect of vasoconstriction was found to have outlasted the secretory effect; the blanching reaction persisted even after the secretion of sweat ceased. But on one point the results of the present experiments differed significantly from those of other workers. In this series none of the subjects showed any evidence of sweating at any stage over a well-defined zone encircling the point of injection (see the Figure). This area devoid of sweating appeared to correspond with the limits of the blanched area.

It has been stressed that the effect of epinephrine and the related substances on the sweat glands appear to be specific. The response, although of lesser magnitude than that produced by acetylcholine, is not the result of injection of the fluid itself, as evidenced by the lack of any such effect of saline alone. Various hypotheses regarding the possible mechanism of adrenergic sweating in human skin have been discussed. These consist of (a) mediation through the central nervous system, (b) systemic alteration of the cardiovascular function, (c) the result of contraction of the myoepithelial cells of the sweat glands, (d) stimulation of the sweat glands by the ischemia produced by epinephrine, (e) ultimate liberation of acetylcholine in the tissues, (f) stimulation of the sudomotor nerve endings, (g) induction through the axon-reflex mechanism, or (h) direct activation of the secretory cells. Experimental evidence has been forwarded by various workers in support of each hypothesis, but nothing has yet emerged to be endorsed as unquestionably acceptable.

Generic and Trade Names of Drug

Phenylephrine—*Neo-Synephrine*.

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