16384 P

Evidence for an Adrenergic Component in the Nervous Mechanism of Sweating in Man.*

HENRY HAIMOVICI.

From the Surgical Division, Montefiore Hospital, New York City.

In the course of an investigation on the vasomotor effects of Dibenamine† (N,N-dibenzyl-β-chloroethylamine hydrochloride), a new adrenergic-blocking agent, it was found that spontaneous palmar sweating in man was inhibited. The interpretation of this observation appeared to be at variance with the known concept of the strictly cholinergic innervation of these glands.

The apparent discrepancy between our observation and the classical concept of the nature of the nervous supply to the sweat glands prompted this investigation.

Methods and Material. A colorimetric method, developed by Silverman and Powell,[1] was used for determining the presence and the amount of sweating. Prints of the sweat glands were obtained on paper treated with tannic acid. The tannic acid reacts with the iron of ferric chloride painted on the skin, to form a stain on the paper ranging from gray-blue to blue-black. The size and intensity of the resulting pattern are directly proportional to the amount of sweat secreted.

Sweat prints of the palms were taken in all instances. Occasionally those of the forehead, cheeks, forearm and plantar region of the feet were also taken. In conjunction with the study on sweat, measurements of skin temperature of the head and the upper and lower extremities were recorded in all cases. These determinations were made under basal conditions. The environmental temperature ranged from 72° to 76°F, with a fairly constant humidity. Sweat prints and thermometric changes were recorded before and after the administration of Dibenamine. The latter was administered by the intravenous route, at the dosage of 5 mg per kg of body weight. The exact details of the method of administration were reported in a previous publication.[2]

The anhidrotic effects of this adrenergic-blocking drug were studied 52 times in 24 subjects, using the colorimetric method. In addition, at the early stage of this investigation, simple clinical observations of the suppression of sweating were made 8 times in 2 other subjects. Eleven of these subjects had essential hypertension, 8 had various vascular conditions, and 7 had various neurological syndromes.

Results. (a) In subjects exhibiting intense or strong spontaneous palmar sweating, Dibenamine administration was usually followed either by total or partial suppression of sweating. In subjects with moderate or faint sweat response patterns, Dibenamine induced in most instances a complete suppression of sweating. Concomitant measurements of skin temperature showed in each case a maximum vasodilation of the cutaneous vessels of the hands and fingers (90° to 94°F).

(b) Intravenous injection of neosynephrine (0.5-1.0 mg) induced moderate sweating. After Dibenamine, neosynephrine remained without effect on the sweat function. Mecholyl (25 mg) given subcutaneously after Dibenamine, induced profuse sweating, mostly on the face and on the dorsum of the hands.

When vomiting, a reflex vagal phenomenon, followed the administration of Dibenamine it was usually accompanied by marked or

* This investigation was supported by the Peripheral Vascular Diseases Research Fund.

† Trademark, Givaudan-Delawanna, Inc. Dibenamine was supplied by the Givaudan-Delawanna, Inc., Delawanna, N.J., through the courtesy of Dr. W. Gump.

1 Silverman, J. J., and Powell, V. E., *Am. J. Med. Sc.*, 1944, **208**, 297.

2 Haimovici, H., and Medinets, H. E., PROC. SOC. EXP. BIOL. AND MED., 1948, **67**, 163.

profuse spontaneous sweating. Within 15 to 30 minutes after cessation of vomiting, however, the anhidrotic effect of Dibenamine became again apparent.

Discussion. The known fact that the sweat glands, although under the control of the sympathetic nervous system, respond to parasympathetic drugs, has long been a puzzle. Dale and Feldberg[3] have shown in the cat that the fibers governing these glands were cholinergic.

In man, parasympathetic drugs alone were known to promote or suppress sweat secretion. Certain types of sweating in man, however, could receive no satisfactory explanation on the basis of the concept of the exclusive cholinergic innervation. Indeed "cold sweat" due to psychic stimulation or that accompanying the so-called sympatho-adrenal attacks in pheochromocytoma, are such examples. In the latter case, there is ample evidence to show that the clinical manifestations are mediated through circulating adrenaline.[4,5] The mechanism whereby sweating is induced under these circumstances does not seem to be in harmony with the cholinergic concept.

The inhibition of sweating induced by Dibenamine appears to be an adrenergic-blocking phenomenon. Indeed, it has been shown, both in animals and man, that Dibenamine inhibits the pressor effect of epinephrine, neosynephrine or that following stimulation of adrenergic fibers.[2,6,7] In addition, myosis in man caused by the administration of Dibenamine is not reversible by epinephrine or paredrine while it is by atropine.[8] These facts indicate that Dibenamine is a specific adrenolytic and sympatholytic drug. It can therefore be assumed that the suppression of sweating by Dibenamine is truly an adrenergic-blocking effect.

The production of sweat by sympathomimetic drugs is a controversial matter. While in certain animals (horse, sheep) epinephrine induces marked sweating,[9,10] in man, it is known to fail to do so. Most investigators, with the exception of Freund[11] are in agreement on this point. However, sweating in man is known to occur after ephedrine[12] and benzedrine.[13]

In this study neosynephrine, a sympathomimetic drug having many similarities to epinephrine, induced moderate sweating. The effect of sympathomimetic agents on sweat function is under further investigation.

The production of sweating by mecholyl, after Dibenamine, indicates that the cholinergic fibers remained unaffected by the latter. This is another evidence of the specific adrenergic-blocking action of Dibenamine.

From the data presented above it appears that, in addition to the known cholinergic fibers supplying the sweat glands, there is also an adrenergic component in the nervous mechanism of sweating in man.

I wish to express my thanks to Drs. Louis Leiter (Medical Division) and H. Houston Merritt (Neuro-Psychiatric Division) for permission to use patients from their respective divisions for this investigation.

The assistance of Dr. H. E. Medinets is acknowledged.

3 Dale, H. H., and Feldberg, W., *J. Physiol.*, 1934, **82**, 121.

4 Beer, E., King, F. H., and Prinzmetal, M., *Ann. Surg.*, 1937, **106**, 85.

5 Goldenberg, M., Snyder, C. H., and Aranow, H., Jr., *J. A. M. A.*, 1947, **135**, 971.

6 Nickerson, M., and Goodman, L. S., *J. Pharm. and Therap.*, 1947, **89**, 167.

7 Haimovici, H., PROC. SOC. EXP. BIOL. AND MED., 1947, **64**, 486.

8 Haimovici, H., unpublished data.

9 Muto, K., *Mitt. med. Fak. Univers. Tokyo*, 1916, **15**, 365 (in Kuno, Y., 9a).

9a Kuno, Y., *The Physiology of Human Perspiration*, London, J. & A. Churchill, Ltd., 1934, 278 pp.

10 Langley, J. N., and Bennett, S., *J. Physiol.*, 1923, **57**, 121.

11 Freund, E., *Wien. klin. Wchnschr.*, 1920, **33**, 1009.

12 Chen, K. K., and Schmidt, C. F., *Medicine*, 1930, **9**, 1.

13 Wilbur, D. L., MacLean, A. R., and Allen, E. V., *J. A. M. A.*, 1937, **109**, 549.