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Effect of Autonomic Blocking Agents on Sweat Secretion in Cat.

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Sweat glands, although innervated by sympathetic postganglionic fibers, are excited by parasympathomimetic drugs (acetylcholine, mecholyl) and blocked by atropine. Dale and Feldberg[1] found that eserinized perfusates collected from the cat's foot during stimulation of the sacral sympathetic ganglia gave positive pharmacological tests for an acetylcholine-like substance. Perfusates collected during stimulation were inactive, if the sweat glands were excluded from the circulation by ligating the base of the footpad. The sudomotor system was thus shown to be anatomically sympathetic, but pharmacologically parasympathetic (cholinergic).

A recent study by Haimovici[2] suggests, in addition, an adrenergic component of sudomotor innervation. He points out that ephedrine, benzedrine and neosynephrine, all sympathomimetic drugs, evoke moderate sweating in man. Using a qualitative colorimetric method for detecting sweat secretion, he noted depression of both spontaneous and neosynephrine-induced sweating in man after injection of Dibenamine (N, N-dibenzyl-β-chlorethylamine hydrochloride), although mecholyl still induced profuse sweating. Since numerous studies indicate that Dibenamine[3] is a specific adrenolytic and sympatholytic drug, he concludes that suppression of sweating by Dibenamine indicates, in addition to the known cholinergic innervation, an "adrenergic component in the nervous mechanism of sweating in man."

In the present experiments the effects of Dibenamine and atropine on sweat secretions in the cat are studied by a quantitative procedure. Electrical stimulation of the lumbar sympathetic chain evokes transient electrical negativity in the skin of the footpad, relative to gland-free skin of thigh, back or ear.[4,5] The potential is the result of sweat gland activity, and its magnitude is a quantitative measure of the number of neuroglandular elements active. The response to a constant single shock to the sympathetic chain is relatively constant over long periods of time, permitting ready recognition of deviations due to injected drugs.

Methods and materials. In 5 cats, anesthetized with sodium pentobarbital, the lumbar sympathetic chain was exposed retroperitoneally. Single square wave shocks, 0.5 msec. in duration and of supramaximal intensity, were delivered to the L5-L6 interganglionic segment of the chain every minute for 5-15 minutes before, during, and for 30 minutes to one hour after drug infusion.

The potentials were recorded through Pb-$PbCl_2$ electrodes attached to the shaved skin of the thigh and to the ipsilateral hind footpad. The latter electrode, designed by pouring lead around a positive plaster impression of a cat's foot, established firm contact with all parts of the hairless foot and toe pads. The potentials were recorded without amplification on a string galvanometer or on a Hathaway galvanometer after amplification by a DC amplifier of the carrier type.*

The Dibenamine solution, prepared freshly in slightly acid saline, was administered through the femoral vein slowly (approximately 1 mg/min.) to avoid the complica-

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

2 Haimovici, H., PROC. SOC. EXP. BIOL. AND MED., 1948, **68**, 40.

3 Nickerson, M., and Goodman, L. S., *Fed. Proc.*, 1948, **7**, 397.

4 Richter, C. P., and Whelan, F., *J. Neurophysiol.*, 1943, **6**, 191.

5 Patton, H. D., *J. Neurophysiol.*, 1948, **11**, 217.

* The amplifier was designed and constructed by Mr. R. S. Bark, Department of Physiology and Biophysics, University of Washington School of Medicine.

tions of precipitous hypotension. Total dosage was recorded at each one-minute interval; final total dosages ranged from 15-20 mg per kilo of body weight. The pilomotor response of the tail to repetitive stimulation of the sympathetic chain was noted at the beginning and end of each experiment to assay qualitatively the effectiveness of the dosage.

Atropine sulfate was given in a similar fashion, except that the total dosage was administered rapidly.

Results. Slow intravenous infusion of Dibenamine in dosages (15 to 20 mg per kg) sufficient to block completely the pilomotor response of the tail, to produce miosis and to relax the nictitating membrane did not diminish the electrical response of sweat glands to preganglionic sympathetic stimulation. Fig. 1 shows the results of a typical experiment. At no time during the infusion did the magnitude of the potential drop below the control value. In some experiments longer post-infusion controls showed that the potentials were maintained at control heights as long as an hour after administration of the full dose. Indeed, in some animals the response increased moderately during and following Dibenamine dosage (Fig. 2). In only one experiment did the response show a significant decrease (35 minutes after full dosage); in this case it was found that the initially chosen stimulus strength was too weak, and the response was restored with increased strength of stimulus.

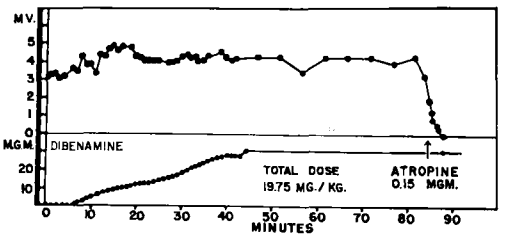

FIG. 1.

Upper graph, magnitude of footpad potential (m.v.) in response to supramaximal sympathetic stimulation. Lower graph, cumulative dose of Dibenamine. At the end of the experiment, injection of atropine rapidly abolished the responses.

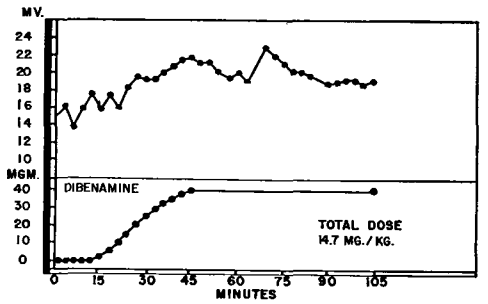

FIG. 2.

Increase in footpad potentials following Dibenamine administration.

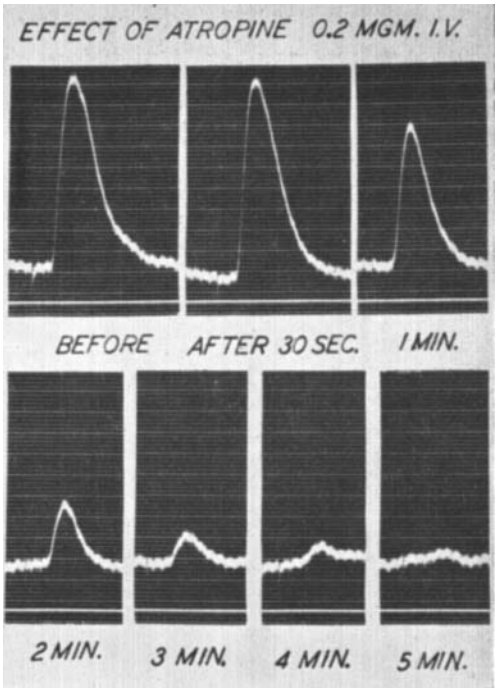

FIG. 3.

Potential responses of footpad to single shock stimulation of the sympathetic chain before and after injection of atropine.

Discussion. The results indicate that sweat secretion in the cat is not blocked by Dibenamine, even with doses 3-4 times as great as that reported to block sweating in man. Miosis, relaxation of the nictitating membrane, and paralysis of the pilomotor system indicated that the dosage was adequate to block known adrenergic systems. In some animals the magnitude of the footpad potential actually increased during infusion of the drug.

This may have been due to vasodilation and increased blood supply to the glands.

On the other hand, irreversible sudomotor paralysis consistently followed injection of atropine. It is thus concluded, in agreement with Dale and Feldberg, that the sudomotor innervation in the cat is entirely cholinergic. Either there exists a marked species difference in cat and man in this respect, or the qualitative methods of observing sweating are misleading.

Summary. The effect of autonomic blocking agents on sweat gland response to single shock excitation of the sympathetic chain was studied in cats by a quantitative and objective method. Dibenamine, an adrenolytic and sympatholytic agent, failed to block sweat secretion whereas atropine consistently produced complete and irreversible sudomotor paralysis. It is concluded that the sudomotor innervation in cat is entirely cholinergic and possesses no adrenergic component, as reported in man.

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Stable, Reduced, Desiccated Streptolysin "O."*

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A technic has been described[1] for the determination of the antistreptolysin "O" titer of serum which involved the employment of a concentrated lysin, diluted and reduced to the active form with a solution of cysteine hydrochloride at the time of use. This method has proved to be very satisfactory. Large amounts of the lysin have been prepared not oftener than every 12 months and deterioration during storage at circa 2°C has rarely been observed. A stable material not requiring refrigeration nor reduction at the time of use would be most desirable. This report describes a procedure for the preparation of a desiccated, reduced streptolysin "O" which, upon reconstitution with distilled water, is immediately ready for use.

Streptolysin. Concentrated streptolysin "O", prepared exactly as described in the paper mentioned above, is used.[1] Complete removal of sulphate ions is determined after dialysis by the addition of a drop of 25 percent barium chloride solution to a small amount of the concentrated material. A precipitate forms after dialysis and the addition of sodium chloride. It should be removed by centrifugation.

Cysteine Hydrochloride. The dry salt is required.

Concentrated Buffer. A concentrated (4 times normal) buffered saline solution is prepared according to the following formula.

	g
NaCl	68.0
KH_2PO_4	45.2
$Na_2HPO_4 \cdot 12\ H_2O$	74.6
Distilled water to make 4 liters.	

After the salts have been dissolved the acidity is checked with a glass electrode pH meter and adjusted to final pH of 6.5. The solution need not be sterilized.

Buffered Solvent for Cysteine. Seven and two-tenths grams of solid NaOH is added to one liter of normal buffered saline (1 part of concentrated buffer saline diluted with 3 parts of distilled water). At the time of reduction and dehydration an M/5 solution of cysteine hydrochloride is prepared by dissolving 3.0 g of the dry salt in 100 cc of this alkaline buffer. Final pH should be 6.5 to 7.2. The solution need not be sterilized.

* This investigation was conducted under the auspices of the Commission on Acute Respiratory Diseases, Army Epidemiological Board, Office of the Surgeon General, United States Army, Washington, D.C.

1 Rantz, L. A., and Randall, E., PROC. SOC. EXP. BIOL. AND MED., 1945, **59**, 22.