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Action of Drugs on Electrical Responses of Slowly Conducting Nerve Fibers.

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It has been shown¹ that faradic stimulation of the attached mesenteric nerves causes inhibition of the movements of excised segments of intestine, and that this effect of electrical stimulation can be prevented by cocaine HCl, 1:50,000, atropine sulfate, 1:1000, nicotine, 1:1000, or ephedrine HCl, 1:10,000. In an effort to explain these actions of the drugs named, we observed their effects on action potentials of splanchnic and vagus nerves of rabbits and the sciatic nerves of frogs. Mammalian nerves were immersed in oxygenated modified Locke's solution at 34° C., frog nerve in oxygenated Ringer solution at room temperature. Measured amounts of stock solutions of the drugs were added to the bath. Action potentials of the nerves were recorded by means of a cathode ray oscillograph and appropriate vacuum tube amplifier. Stimulation was by a single dry cell and Harvard inductorium. Electrodes were of platinum. To obtain a record, a nerve was removed from the bath and laid across the electrodes. Records were made before the nerve was drugged, at intervals after adding the drug, and again after allowing recovery of the nerve in fresh Locke's solution. Attention was paid particularly to the "C" wave, since this was thought to represent that type of fibres responsible for intestinal inhibition. The wave was recognized by stimulation required, by amplitude of the wave and by its rate of conduction along the nerve.

Thirty to 45 minutes treatment with cocaine HCl 1:40,000 to 1:20,000 or by atropine sulfate 1:1000 or nicotine 1:1000 resulted in disappearance of the "C" wave (31 tests). This was interpreted to mean that non-medullated and finely medullated nerve fibres were paralyzed by such treatment. Return to fresh bath permitted recovery. Nicotine 1:5000 failed to change the action potential, but atropine sulfate in similar concentration caused disappearance of the C wave in one of 3 nerves tested. Ephedrine HCl 10^{-4} abolished the C wave of 2 nerves, decreased the rate of conduction and amplitude of the wave of 4 nerves and failed to alter one nerve. In higher concen-

¹ Hendricks and Thienes, *Proc. Soc. Exp. Biol. and Med.*, 1931, **28**, 993.

tration (1:1000 to 1:3000) 8 nerves were paralyzed, 9 slightly depressed and 2 unchanged.

Conclusions. Very dilute concentrations of cocaine HCl depress slowly conducting nerve fibres; in higher concentration, a similar depression is produced by ephedrine HCl, atropine sulfate or by nicotine base.

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Effect of Cortical Extract on Glucose Tolerance of Adrenalectomized and Hypophysectomized Rats.

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In previous work¹ we found that the ability of the hypophysectomized rat to remove excess sugar from the blood stream decreased with time after operation. This gradual decrease in ability to remove excess sugar indicated that the effect must be due to the progressive atrophy or derangement of some other organ following removal of the pituitary body. We gave our first attention to the rôle of the adrenal gland in this effect since Leloir² had shown a decrease in the rate of removal of glucose from the blood in adrenalectomized dogs, associated with decreased glycogen formation.

To test this possible connection the following groups of male rats were given 0.125 gm. glucose per 100 gm. body weight by injection of 50% solution into the saphenous vein:

- a. Normal control animals.
- b. Normal animals injected with 0.2 cc. Wilson's adrenal cortex extract per day.
- c. Young adult animals adrenalectomized 6 days previously.
- d. Similar adrenalectomized animals injected with 0.2 cc. extract per day for the previous 4 days.
- e. Hypophysectomized animals, operated on 17 days previously.
- f. Similar hypophysectomized animals injected with 0.2 cc. extract per day for the previous 6 days.

All animals were fasted for 24 hours before receiving the glucose

¹ Samuels, L. T., and Ball, H. A., *Endocrin.*, in press.

² Leloir, L. F., *Suprarrenales y Metabolismo de los Hidratos de Carbono*, Buenos Aires, 1934.