

Aside from the fact that with this vessel the resting respiration of the tissue may be first determined in the complete absence of cyanide, there is the further advantage that any escape of cyanide into the alkali of the inset must take place by diffusion through the medium bathing the tissue. The latter point appears to be of considerable importance for, as shown in Table I, with this method the inhibitions obtained with tissues such as kidney, stomach and intestine are considerably higher than those usually reported for these tissues. For example Dixon and Elliott² and Muntwyler and Binns³ obtained a maximum inhibition of 60-80% for these tissues whereas with this method, inhibitions of 85-95% have been obtained regularly with 0.01 to 0.05 M NaCN. In view of the convenience of this method and the considerably higher degree of inhibition obtained with it as compared with the conventional method it has been adopted in this laboratory for all experiments on the effect of cyanide or other volatile reagents upon tissue respiration.

8638 P

Action of Drugs, Nerves and Electric Current in Iris Sphincter.

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It was thought that electrical stimulation might help to locate the site of action of a neural hormone.

A ring or strip a few millimeters wide was cut from the pupillary margin of the iris, usually of a cat, and hung to a writing lever between platinum electrodes in a modified Locke solution of pH 7.4, warmed to about 37°C. The sphincter thus isolated was stimulated electrically, usually for about 5 seconds at a time, with a faradic current from a Harvard inductorium using 3 fresh dry cells in the primary.

The accompanying sample tracing illustrates the findings that:

Electrical stimulation, 1E, of the isolated sphincter muscle caused a contraction followed by a much greater relaxation. This suggests that the electric current "stimulated" first a contractor re-

² Dixon, M., and Elliott, K. A. C., *Biochem. J.*, 1929, **23**, 812.

³ Muntwyler, E., and Binns, D., *Am. J. Physiol.*, 1934, **108**, 80.

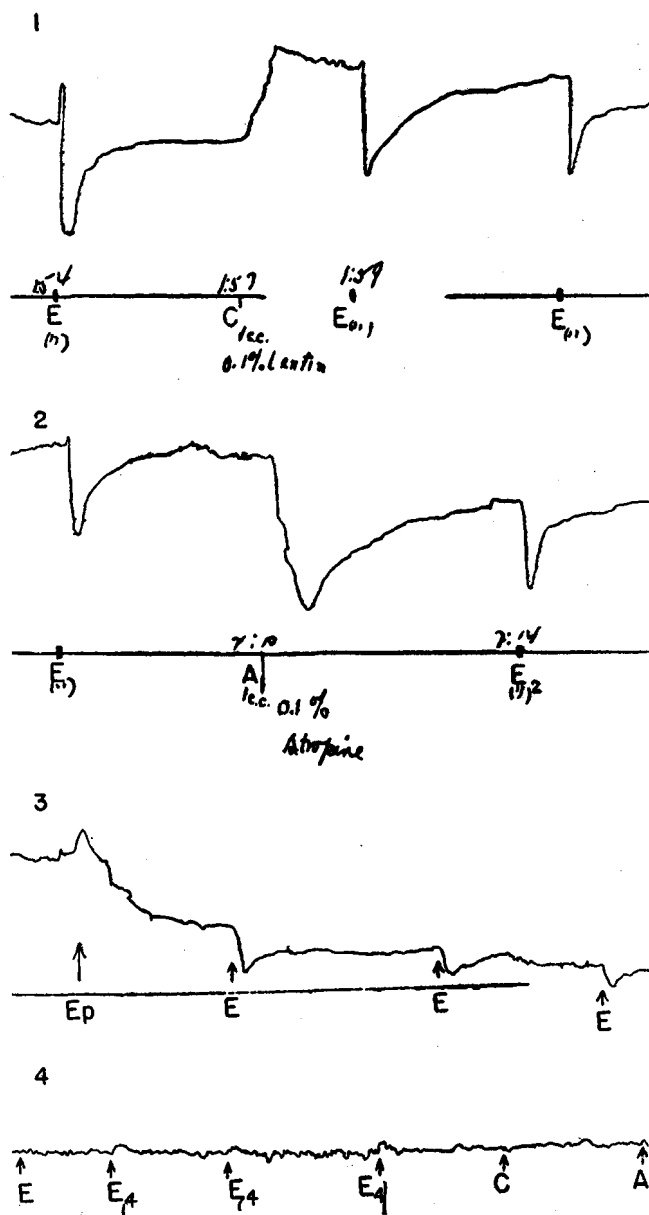


FIG. 1.

Photostat of tracing, retouched. Series 2, Exp. 20, Cat No. 14, 1/29/36. E, Elect. Stim., coil Dist. 6, for 5 sec.; C, 1 cc. of 0.1% Carbam. Chol.; A, 1 cc. Atrop., 0.1%; Ep, 1 cc. Epineph., 1:10,000, *Segment 4* follows two more doses of Epineph. Here the base line is level with the tracing. E4, Elect. Stim. w. C. D. 4 cm. The minute waves represent spontaneous contractions or tremor of the apparatus.

ceptive substance and then a relaxor receptive substance in the sphincter muscle.

Carbaminoyl choline, 1C, now produced a sustained contraction, and electrical stimulation still produced a contraction with much greater relaxation. Since this choline ester, in this concentration, does not act on nerve endings (Shaklee and Christensen¹), the action must be on the contractile mechanism or on some other substance in the muscle fiber.

Atropine, 2A, after the choline ester, caused the disappearance of both contractions, *i. e.*, that produced by the choline ester and that produced by electrical stimulation. The inference seems to be that atropine inhibited the contractor receptive substance, upon which both the choline ester and the electric current seem to act. Electric current, 2E₂, after the atropine, caused only relaxation and about as much as before the drugs had been applied. This would seem to indicate that neither the choline ester nor the atropine, present in the bath, was affecting the contractile mechanism directly, or the relaxor receptive substance; hence they must have acted on the contractor receptive substance.

Epinephrine, 3Ep, added to the choline ester and atropine, already in the bath, caused a further relaxation, presumably by "stimulating" the relaxor receptive substance upon which the electric current had been acting. *Excess* epinephrine caused a disappearance of the relaxation due to electric current, 4E. From this, one might infer that excess epinephrine exhausted or inhibited the relaxor receptor substance upon which it and the electric current had been acting.

Increased electric current, 4E4, after both the contractor and the relaxor receptive substances had been inhibited by atropine and epinephrine, caused a slight contraction followed by an equal relaxation. Since the receptive substances had been nullified and since the contraction was followed by an equal relaxation, this contraction seems to be due to direct stimulation of the contractile mechanism by the electric current.

The increase in length of the muscle after atropine and epinephrine suggests that most of the normal tone of isolated smooth muscle is due to spontaneous catalysis of the receptor substance.

In this study we have used eyes from 46 cats, 2 rabbits and 2 pigs. Further details will follow.*

¹ Shaklee, A. O., and Christensen, K., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1619.

* We are grateful to Merck and Co., for the carbaminoyl choline.

Summary: The results of electric stimulations of an isolated smooth muscle before and after the successive applications of a choline ester, atropine and epinephrine, seem to lend support to the theory that these drugs and the electric current, in ordinary strengths, act solely on receptive substances for the neural hormones. These findings are in harmony with the chemical theory of nerve transmission, and, taken with the findings of others, suggest that each axone in the body acts by liberating at its endings a specific substance that catalyzes a specific receptive substance in the effector or other nerve cell with which they lie in contact, into fractions, one of which directly stimulates or inhibits the effector mechanism, or, in the nerve cell, the impulse mechanism. The experiments of Láncoz² suggest calcium ions as one of these fractions, those of Brown and Feldberg³ suggest potassium ions as another.

8639 C

Influence of Estrone upon Galactin Content of Male Rat Pituitaries.*

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McQueen-Williams¹ has demonstrated that one normal male rat pituitary contains sufficient galactin to induce a good response in a one-month-old pigeon when implanted subcutaneously over the crop gland. Better results have been obtained in our laboratory by injecting the macerated pituitary intradermally over the crop gland as described by Lyons and Page.²

In order to study the effect of estrone upon the galactin content of male rat pituitaries, 16 animals were paired upon the basis of body weight. One of each pair was injected subcutaneously daily for 15 days with 500 International Units of the benzoate of hy-

² Láncoz, Anna, *A. f. Exp. Path. u. Pharm.*, 1936, **180**, 312.

³ Brown, G. W., and Feldberg, W., *J. Physiol.*, 1936, **86**, 10P.

* Contribution from the Department of Dairy Husbandry, Missouri Agricultural Experiment Station, Journal Series No. 464.

¹ McQueen-Williams, M., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **33**, 406.

² Lyons, W. R., and Page, Emery, *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 1049.