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A Pharmacological Study of the Inhibitory Mesenteric Nerves to the Intestine.*

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An attempt to understand better some of the actions of cocaine, ephedrine and other drugs on the intestine, led to the use of the excised nerve-muscle preparation of the intestine described by Thomas.¹ At the time our experiments were begun, McSwiney and Robson² had reported the use of a similar preparation of the stomach, and since then there have appeared papers by Finkelmann³ and McSwiney and Robson,⁴ describing results with the nerve-muscle preparation of the intestine. Our results in general confirm those of the authors mentioned, and extend the study further.

A modified Locke solution was used to immerse the tissues, which were removed as required from rabbits and dogs anesthetized with urethane and chloretone or with amytal. Records were made of the movements of only the longitudinal muscle fibres. Stimulation of the mesenteric nerves was by means of the Harvard inductorium, through platinum electrodes applied to the periarterial nerves. Slowly repeated shocks (1 to 10 per second), as well as rapid shocks (12 to 60 per second), and minimal effective as well as supermaximal strength, stimulating for periods up to 1 minute, resulted only in decrease in tone and inhibition of the movements of the intestinal muscle. The inhibition persisted for several seconds after stimulation ceased, and in a few instances, there was over-recovery of tone, with gradual return to normal, thus confirming the results of Thomas.¹ All effects of nerve stimulation were closely imitated by epinephrine on each individual preparation. In no instance did a primary augmentation of intestinal activity result from nerve stimulation.

The inhibition was not prevented by nicotine or atropine in 1:10,000 concentration, or by a mixture of nicotine and atropine, each 1:10,000. Ergotamine tartrate or ergotamine methane sul-

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¹ Thomas, J. E., *Am. J. Physiol.*, 1926, **76**, 228.

² McSwiney, B. A., and Robson, J. M., *J. Physiol.*, 1929, **68**, 124.

³ Finkelmann, B., *J. Physiol.*, 1930, **70**, 145.

⁴ McSwiney, B. A., and Robson, J. M., *J. Physiol.*, 1931, **71**, 194.

phonate[†] 1:150,000 to 1:75,000, ephedrine-HCl 1:20,000 to 1:10,000, cocaine-HCl 1:75,000, nicotine 1:1,000, atropine 1:1,000 and a mixture of nicotine and atropine, 1:1,000 each, markedly diminished or entirely abolished the inhibitory effect on intestinal movements of electrical stimulation of the mesenteric nerves.

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An Analysis of the Actions of Cocaine on Excised Smooth Muscles.*

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In a previous report¹ there was presented evidence that cocaine is not a general sympathomimetic drug. Since most of the studies of the action of this drug on the iris (Gold, Miller, Koppanyi, Yonkmann²) indicate an action on the terminal mechanism of the sympathetic nerves to this organ, a further analysis of the action of cocaine on other organs was carried out. All studies were on excised tissues bathed in Tyrode solution or modified Locke solution. The tissues were taken from animals killed by a blow, or under urethane and chlorethane or amytales anesthesia. Only experiments on small intestine, colon and uterus of the rabbit are described in this report.

Small intestine. Five segments of small intestine of the rabbit were shown to respond to 1:10,000 cocaine HCl by contraction. This action was not prevented by previous treatment of the tissue with nicotine and atropine, 1:50,000 each. Of 15 segments which were depressed by cocaine 1:10,000, 5 were depressed by cocaine after nicotine and atropine 1:20,000 each, 5 were depressed by cocaine, but not by epinephrine, after ephedrine 1:10,000, and 5 were depressed by cocaine, but not by epinephrine, after ergotamine, 1:75,000. These concentrations of ephedrine and ergotamine were shown to prevent the inhibitory effect of electrical stimulation

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¹ Thienes, C. H., *J. Pharm. Exp. Therap.*, 1928, **33**, 21.

² Gold, H., *J. Pharm. Exp. Therap.*, 1924, **23**, 365; Miller, G. H., *Ibid.*, 1926, **28**, 219; Koppanyi, T., *Ibid.*, 1930, **38**, 113; Yonkmann, F. F., *Ibid.*, 1930, **40**, 195.