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The Effect of Ergotamine on Intestinal Motility.

WILLIAM SALANT. (With the technical assistance of H. Nagler and Leon Herbert Ehrlich.)

From the Biological Laboratory, Cold Spring Harbor, L. I., N. Y.

According to Mendez[1] ergotamine produced depression of motility in the isolated intestine of the rabbit. Later Issekutz and Leinzinger[2] reported that it was without effect on the intestine of these animals. More recently Rothlin[3] stated that ergotamine produced no effect in some rabbits and caused decreased motility in others. He also reported that in experiments with ergotamine on the intestine *in situ* of dogs his results were negative. Planneles[4] observed in the guinea pig that the isolated intestine of these animals was depressed by ergotamine. Thienes[5] recently carried out experiments on the isolated intestine of the guinea pig, rabbit and cat with adrenalin and low concentrations of ergotamine (1:250,000 and 1:500,000). He made no statement, however, of the action of ergotamine but a tracing of the intestine of a rabbit shows that no change in motility occurred as a result of the treatment with ergotamine. In the course of studies on the effect of intestinal motility[6] in which ergotamine was occasionally employed, it was noticed that the intravenous injection of the substance stimulated peristalsis in cats under urethane anesthesia. More extensive observations carried out since fully corroborated our earlier findings, and we were able also to show that the increase in the motor functions was in some cases very striking. These studies, which were carried out by the Trendelenburg method, on the intestine *in situ* were extended to experiments on the isolated intestine of the cat, suspended in oxygenated Locke's solution and kept at body temperature. Ergotamine in concentration of about 1:200,000 to 1:500,000 produced depression, the tonus being slightly decreased and the rhythmic movements were abolished or greatly diminished in force and frequency. As the results might have been due to a substance liberated when ergotamine was injected into the circulation, blood was obtained from treated animals, defibrinated, added to an equal volume of Locke's solution

[1] Mendez, *J. Pharmacol. and Exp. Therap.*, 1927, xxxii, 451.

[2] Issekutz and Lenzinger, *Arch. Exp. Path. u. Pharmakol.*, 1928, cxxviii, 165.

[3] Rothlin, *J. Pharmacol. and Exp. Therap.*, 1929, xxxvi, 657.

[4] Planneles, *Arch. Exp. Path. u. Pharmakol.*, 1929, cv, 38.

[5] Thienes, PROC. SOC. EXP. BIOL. AND MED., 1929, xxvi, 501.

[6] Salant and Brodman, *J. Pharmacol. and Exp. Therap.*, 1929, xxxvii, 55.

and the action of ergotamine was then tested. The results after adding ergotamine were not constant, showing in some cases stimulation, in some depression. But in experiments in which defibrinated blood from untreated cats was mixed with Locke's solution ergotamine produced the same effects. Indeed, our tracings in one series of experiments showed, on the contrary, that moderate but distinct stimulation was produced by ergotamine

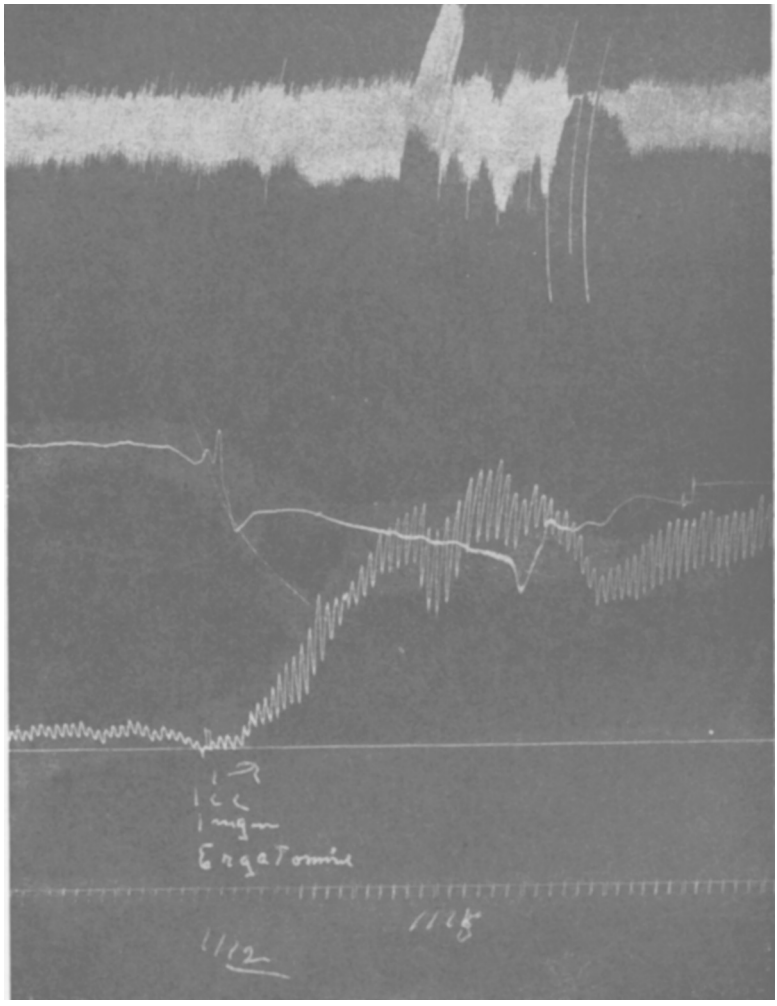

FIG. 1.

Experiment 773, female cat, wt. 2.8 K., urethane anesthesia. One mg. ergotamine injected intravenously stimulated the intestine. Tracings from above downward show respiration, blood pressure, intestinal movement. Time in tenth seconds and minutes.

in concentration of 1:250,000 to 1:50,000 or even 1:25,000. The blood probably contained, therefore, a substance (or substances) that modified the action of ergotamine.

We are very much indebted to Mr. Eugene Marti of the Sandoz Company for a generous supply of ergotamine, gratis, used in this and other experiments by the writer.

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The Reversal of Action of Ergotamine by Calcium and Changes in C_H.

WILLIAM SALANT AND HAROLD NAGLER.

From the Biological Laboratory, Cold Spring Harbor, L. I., N. Y.

As stated in the preceding communication,[1] the response of the intestine to ergotamine has been studied in different animals. No observations have been made, however, to determine whether changes in ionic content of the surrounding medium modified the action of ergotamine. We, therefore, undertook the investigation of this problem and selected the intestine of the rat for the test object. As far as we know, no studies with ergotamine on the intestine of this animal have been reported. The experiments of Rosenmann,[2] however, are of interest in this connection. He observed that ergotoxin produced stimulation in the isolated intestine of the rat.

Our experiments were carried out by means of the Magnus method, segments of different parts of the intestine being suspended in oxygenated Locke solution maintained at almost uniform temperature, usually 37.5° C. The variations which sometimes occurred seldom exceeded 0.2° C. We found that concentrations of 1:100,000 and sometimes 1:1,000,000 ergotamine in Locke solution with a pH of about 7.2 or 7.3 and containing 0.014% calcium chloride, produced a considerable decrease of tonus, the relaxation being more marked in the ileum and colon than in the duodenum. The rhythmic movements, however, were usually stimulated, especially the amplitude. When the amount of calcium in the solution was increased to 0.028 or 0.056% a striking change in the action of ergotamine occurred when the H-ion concentration was decreased below neutral-

[1] Salant, William, PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, —?

[2] Rosenmann, *Z. f. i. ges. Exp. Med.*, 1922, xxix, 334.