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Ergotamine Tartrate in Experimental Vascular Hypertension Associated with Increased Intracranial Pressure.

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(Introduced by O. H. P. Pepper.)

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Following the intracisternal injection of colloidal kaolin, the rat will develop arterial hypertension associated with increased intracranial pressure.^{1, 2} For the sake of brevity, we shall refer to such an animal as a kaolin-hypertensive rat. The elevation of blood pressure was interpreted as being the result of hyperactivity of the vasoconstrictor center in consequence of the increased intracranial pressure.

Because ergotamine is known to paralyze peripheral parts of the sympathetic nervous system, it seemed possible that this substance might influence arterial hypertension so produced. Hogler³ has reported no lowering of the blood pressure by ergotamine tartrate when given in the dose of one mg to dogs made hypertensive by kaolin. However, Hogler's first blood pressure readings were taken one hour after the injection of ergotamine tartrate so that a transitory effect might have been overlooked.

In addition to producing prolonged hypertension associated with increased intracranial pressure, we also elicited an acute type by introducing physiologic saline into the cisterna magna at a measured pressure. This afforded a second type of test animal for investigating the effect of ergotamine.

Normal and kaolin-hypertensive albino rats were used. Light, uniform ether anesthesia was employed for all procedures. Blood pressure determinations were made by an indirect method previously described.⁴ Ergotamine tartrate† was given intraperitoneally in the dose of 0.05 mg per 100 gm body weight.

Ten normal rats were injected with ergotamine tartrate, the blood

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¹ Griffith, J. Q., Jr., Jeffers, W. A., and Lindauer, M. A., *Am. J. Physiol.*, 1935, **113**, 285.

² Griffith, J. Q., Jr., Jeffers, W. A., and Lindauer, M. A., *Am. J. Physiol.*, 1935, **118**, 1.

³ Hogler, *Klin. Wchnschr.*, 1934, **13**, 241.

⁴ Griffith, J. Q., Jr., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 394.

† The ergotamine tartrate was supplied by the Sandoz Chemical Works, Inc.

pressure being followed for approximately 10 minutes before and for at least 30 minutes after the injection. No effect on blood pressure was noted.

Thirteen kaolin-hypertensive rats were similarly treated. In every instance there was a marked but transitory fall in the blood pressure (35-160 mm Hg). (Fig. 1.)

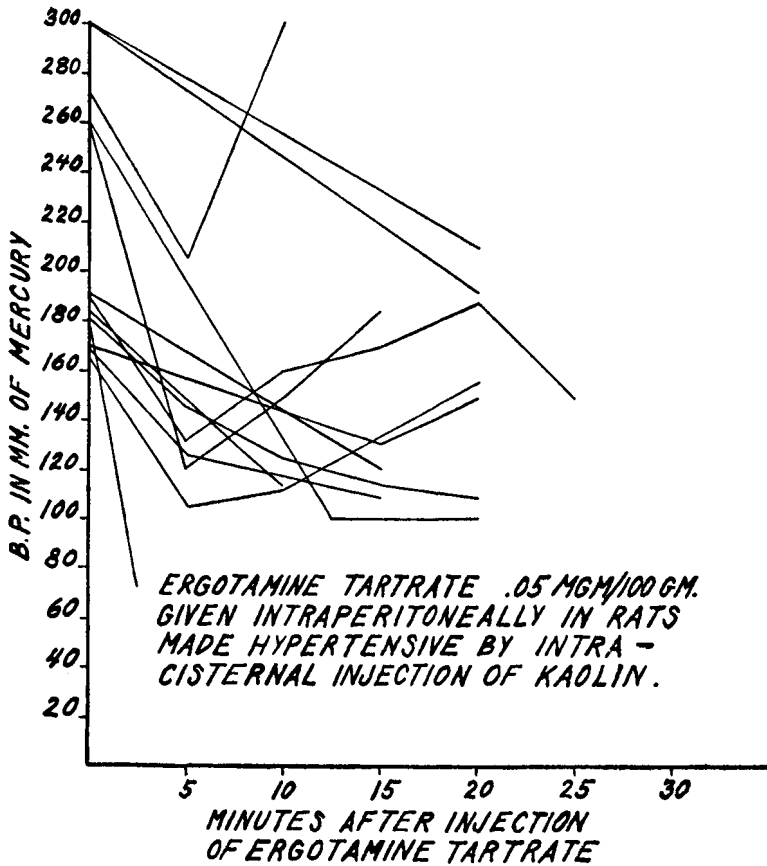


FIG. 1.

As a control, 5 kaolin hypertensive rats were given intraperitoneal injections of a solution of sodium citrate and citric acid of the same pH as the ergotamine tartrate solution (pH 4.2) and their blood pressure followed as above. One animal showed a rise in blood pressure, three showed a slight fall and one a more marked fall (an immediate drop of 23 mm Hg) but this one had been under ether for 21 minutes before the intraperitoneal injection was given.

In 3 normal rats, cerebrospinal fluid pressure was raised to 200-

270 mm of water by introducing physiologic saline into the cisterna magna. The blood pressure rose from 120-130 to approximately 200 mm of Hg. After ergotamine tartrate, all 3 showed an abrupt fall in the blood pressure, 2 dying in 1 to 2 minutes, while in the third, the blood pressure fell from 190 to 100 in 4 minutes, but in the next 12 minutes, rose steadily to the original 190, where it remained for another 10 minutes, after which the experiment was discontinued.

Electrocardiograms were taken on 4 kaolin-hypertensive rats before and after the administration of ergotamine tartrate. There was no immediate slowing of the heart rate. Three of the rats showed slowing (85-200 beats, 15-33%, per minute) 20-30 minutes after ergotamine was given.

Ergotamine tartrate lowers transiently the high blood pressure associated with increased intracranial pressure in the rat. A peripheral vasomotor depression or paralysis, which ergotamine tartrate has been shown to induce under various circumstances, and which may become obvious only in the presence of increased sympathetic constrictor activity, would appear to be a likely explanation.

The electrocardiographic findings were interpreted as evidence that the immediate fall in blood pressure was not due primarily to a cardiac depressant effect of ergotamine.

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Effect of Adrenal Vein Ligation and Pancreatectomy on Metabolism of Renal Tissue.

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Previous reports^{1, 2} reveal that ligation of the lumbo-adrenal veins results in an amelioration of experimental diabetes as evidenced by diminished glycosuria and ketonuria and a basal R.Q. elevated above the diabetic level. The present experiments were conducted in order to determine the ability of renal cortex to utilize carbohydrate. Renal tissue from diabetic animals is incapable of utilizing added glucose

¹ Fazekas, J., Himwich, H. E., and Martin, S. J., *Proc. Soc. Exp. Biol. and Med.*, 1937, **37**, 361.

² Fazekas, J., Himwich, H. E., and Martin, S. J., *Science*, 1938, **87**, 144.