tentiation of other sympathomimetic drug effects by morphine is being investigated.

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Studies on the Emetic and Anti-Emetic Actions of Ergotamine.

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Eggleston and Hatcher[1] showed that intravenous doses of 60.0 mg. of fluid extract of ergot (in terms of the dry drug) produced prompt emesis in the dog, whereas oral administration of even massive doses failed. Eviscerated dogs also showed emesis following intravenous doses. The authors concluded that ergot has a central emetic action. Hatcher and Weiss[2] apparently rejected this supposition, stating "that ergotoxin has no perceptible effect directly on the vomiting center, and that any inhibition by it of the emetic action of substances used in these experiments, must be due to its causing depression of some peripheral structure."

These authors found that massive doses of ergotoxine prevented the emetic action of apomorphine, aconitin, digitalis, and pilocarpine by systemic administration, but not of large oral doses of mercuric chloride and tartar emetic. They concluded that the anti-emetic activity of ergotoxine is due to its depression of afferent sympathetic nerve ends.

Koppanyi[3] found a close parallelism to Hatcher and Weiss' results. His dogs, whose medullary vomiting centre was removed by ablation or depressed by local application of morphine, also failed to vomit following systemic administration of apomorphine, pilocarpine, digitalis, but vomited upon oral administration of tartar emetic, copper and zinc sulphate, and mercuric chloride.

The following experiments were performed to correlate the above findings. Doses are given in mg. × kilogram body weight. In dogs the intravenous administration of small doses (0.02-0.2 mg.) of ergotamine tartrate elicit repeated retching and vomiting, but large doses (0.5 mg. or higher) fail to produce retching or vomit-

[1] Eggleston, C., and Hatcher, R. A., *J. Pharm. and Exp. Therap.*, 1915, **7**, 225.
[2] Hatcher, R. A., and Weiss, S., *J. Pharm. and Exp. Therap.*, 1923, **22**, 139
[3] Koppanyi, T., *J. Lab. and Clin. Med.*, 1930, **16**, 225.

ing. In cats the minimum emetic doses are somewhat lower than in dogs (0.01-0.02 mg.) and doses of 0.3 mg. or higher fail to produce emesis. Dr. F. F. Yonkman of Boston University also has noted the emetic response to small intravenous doses in dogs. (Oral communication.)

In 2 dogs we failed to produce vomiting by application of ergotamine tartrate (0.03 mg.) on the Thumas centre. In 2 experiments we found that the minimum emetic dose is lower when injected into the externalized common carotid artery than when it is given intravenously. Application of larger doses (0.2 mg.) on the centre suppressed the usual vomiting responses following optimum intravenous doses of ergotamine tartrate and also of apomorphine. However, these dogs vomited following oral administration of copper sulphate.

Similarly, the subcutaneous injection of 20 mg. morphine sulphate inhibited ergotamine and apomorphine vomiting, but did not suppress copper sulphate emesis.

In each of 3 dogs we performed a bilateral vago-sympathectomy and transection of the spinal cord at the level of the second thoracic vertebra. Allowing sufficient time for recovery, each of them received an intravenous dose of 0.05 mg. ergotamine tartrate. In every instance the dogs vomited in 3½, 6, and 7 minutes after administration and several times after. Intravenous doses of 0.5 mg. pilocarpine hydrochloride also produced repeated retchings and vomitings.

These results require little interpretation. We are convinced that ergotamine and other systemically administered emetics act directly on the vomiting centre and that the lowering of the threshold of the vomiting centre to normal emetic impulses has little, if any, rôle in the production of "central emesis". Moreover, we feel the inhibition of vomiting by ergotoxine or ergotamine is due to depression of Thumas' centre, but not to paralysis of peripheral afferent structures.

The possible therapeutic applications of these data and a standardization of *Fluidextractum Ergotæ* by the minimum effective emetic doses are being investigated.