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Studies on the Evacuant Action of Ergotamine.

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The studies of Hatcher and Weiss[1] and of Koppanyi[2] suggested the presence of a medullary defecation center, or at any rate, the existence of a non-peripheral control of defecation.

Investigating the gastro-intestinal actions of graded doses of ergotamine tartrate in intact, unanesthetized dogs and cats, we observed certain facts which further support the assumption of a central control of defecation.

Dogs and cats strain and defecate rather promptly following small or moderate intravenous doses of ergotamine tartrate. Doses are given in mgm. × kilogram body weight. In the dog doses of 0.02-0.2 mg. produced prompt and repeated straining and defecation, whereas doses of 0.5 mg. or above were effective only after a considerable delay. (10 min.) In cats, doses of 0.01 and 0.015 mg. also produced straining and defecation whereas doses of 0.1 mg. or higher either produced no defecation or a very delayed response (9-68 min.). Thus in cats the optimum effective doses are somewhat smaller than in dogs. It is also to be noted that there is a close correlation between the evacuation and emetic response produced by ergotamine tartrate. In practically every case where vomiting was produced, defecation also took place and when vomiting did not take place the animals either failed to defecate or evacuation ensued after considerable delay (peripheral effects?).

In 2 dogs we failed to produce defecation by application of ergotamine tartrate (0.03 mg.) on the floor of the fourth ventricle; but the application of larger doses (0.2 mg.) upon the floor inhibited the usual evacuation following optimum intravenous doses. Similarly, the subcutaneous injection of 20 mg. of morphine sulphate eliciting the usual immediate evacuant response, inhibited the evacuant effects of subsequent intravenous doses of 0.1 mg. of ergotamine tartrate.

In each of 3 dogs we performed a bilateral vago-sympathectomy and a high thoracic transection of the spinal cord at the level of the second thoracic vertebra. Allowing ample time for the animals to

[1] Hatcher, R. A., and Weiss, S., *J. Pharmacol. and Exp. Therap.*, 1923, **22**, 139.
[2] Koppanyi, T., *J. Lab. and Clin. Med.*, 1930, **16**, 225.

recover from the effects of anesthesia, each of them received an intravenous injection of 0.05 mg. of ergotamine tartrate. In every instance these injections failed to elicit defecation. However, upon intravenous injection of 0.5 mg. of pilocarpine hydrochloride defecation followed 3, 5, and 9 minutes after administration.

Not wishing to deny the probability of peripheral purging effects of ergotamine and other ergot principles on the intestine, we are even ready to attribute all our delayed or late defecation responses to such an action. We must insist, however, that the extraordinary prompt response to small optimum doses is due to central action, as such responses are inhibited by application of ergotamine tartrate to the medulla, by administration of large doses of morphine, and by simultaneous vagotomy and high transection of the cord.

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Relative Susceptibility of Adult and Young Mice to Asphyxiation.

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It is generally stated that in carbon monoxide asphyxiation the smaller and the younger individuals, with the more active metabolism, tend to approach saturation more rapidly, and that small individuals therefore succumb sooner than large individuals. Four parts of carbon monoxide in 1000 parts of air are considered fatal to man after an exposure of less than one hour and presumably much more fatal to smaller animals such as mice.

Following the observation by one of us (R.C.A.) that the young of a family of wild mice survived while the parents died when exposed to illuminating gas, a series of experiments with 73 white mice was carried out.

The data in Table I show that, contrary to current belief, the younger survive longer. In pure concentrations of chemically inert gases (nitrogen, hydrogen and argon) the young survive exposures from 3 to 6 times as long as those which prove fatal to adults.

The lethal periods of exposure for adult and young mice, in the case of pure CO_2 and CO lie so close together that it is difficult to observe a survival of the young. This is partly due to the fact