

6274

Synergism of Morphine and the Mydriatic Alkaloids in the Albino Rat.

THEODORE KOPPANYI.

From the Department of Pharmacology and Materia Medica, Georgetown University School of Medicine, Washington, D. C.

The subcutaneous or intraperitoneal injection of 10 to 15 mg. of morphine sulphate per 100 gm. of body weight, causes under normal circumstances, no perceptible change in the size of the pupil of the albino rat. Such doses of morphine produce a state of catalepsy and stiffness of the tail in the experimental animal and abolish the corneal reflex.

To such morphinized animals several mydriatics were administered by different routes. At first, only sympathetic stimulants were used. Normal-control and morphinized rats were each given intermuscular injections of cocaine hydrochloride 10 mg. per 100 gm. of body weight. Solutions of cocaine (1:50), of adrenalin hydrochloride (1:1000), and of ephedrine sulphate (1:100) were instilled in the conjunctival sac. (In every series of experiments 12 rats were used.) These installations, or injections, produce no, or only slight, dilatation of the pupil in the normal untreated rats, but increase the size of the pupil from $\frac{1}{2}$ to 4 mm. or more in the morphinized animals.

In another series of experiments, one drop of a 0.002% solution of atropine sulphate was instilled into the conjunctival sac. This installation produced no appreciable change in the normal pupil, but a 60% dilatation in the morphine-treated rats.

Since it is known that morphine causes a secretion of adrenalin from the adrenal gland, it was supposed that this exaggeration of the action of mydriatics by morphine is due to the adrenalin liberated into the blood stream and thus represents a case of additive effects. However, complete adrenalectomies carried out in 25 rats do not support this contention. Adrenalectomized rats under the influence of morphine are just about as sensitive to mydriatics as unoperated controls.

The depression of rats by chloral hydrate or paraldehyde does not enhance the mydriatic effects of adrenalin, cocaine, ephedrine or atropine.

We are forced to conclude that morphine potentiates mydriatic actions especially of sympathetic nature in the albino rat. The po-

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

6275

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

THEODORE KOPPANYI AND EVERETTE I. EVANS.

From the Department of Pharmacology and Materia Medica, Georgetown University School of Medicine, Washington, D. C.

Eggleston and Hatcher¹ 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 Weiss² 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.

Koppanyi³ 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. \times 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.