

Illinois Branch.

Medical and Dental Arts Building, Chicago, May 15, 1929.

4502

Influence of Various Chemical Agents on the Absorption of Histamine From the Intestine.

LAMBERT F. MAMMOSER AND T. E. BOYD.

*From the Department of Physiology and Pharmacology, Loyola University
School of Medicine, Chicago, Illinois.*

Histamine has been shown to be present in the intestinal contents of man and of some other mammals. In view of its powerful pharmacological effects, the question of its absorption has received considerable attention. It can be absorbed from the intestine of the cat in sufficient amounts to produce a marked lowering of blood pressure.¹ Under similar conditions, however, the blood pressure of the dog is not affected.² In man as much as 225 mg. has been taken by mouth with no noticeable effect except a moderate stimulation of gastric secretion.³ It has not thus far been shown that any pathological condition materially affects the behavior of the intestine toward histamine. Previous workers have studied the effects of temporary interruption of the blood supply,¹ of intestinal obstruction, and of distention,⁴ with negative or inconclusive results.

Spadolini⁵ treated the mucosa of the dog's intestine with diluted chloroform, and observed symptoms which he attributed to an increased absorption of the products of bacterial decomposition of proteins. There was, however, no direct evidence of such a change in permeability toward any specific substance. We have studied the effect of chloroform, and of a number of other agents, on the absorption of histamine.

¹ Meakins, J., and Harington, C. R., *J. Pharm. Exp. Ther.*, 1923, xx, 45.

² Koessler, K. K., and Hænke, M. T., *J. Biol. Chem.*, 1924, lix, 889.

³ Ivy, A. C., and Javois, A. J., *Am. J. Physiol.*, 1925, lxxi, 604.

⁴ Wangensteen, O. H., and Loucks, M., *Arch. Surg.*, 1928, xvi, 1089.

⁵ Spadolini, I., *Arch. fisiol.*, 1924, xxii, 435.

In small dogs, under barbital anesthesia, a rubber catheter was passed down into the duodenum from the stomach. A ligature around the pylorus fixed the catheter in place and prevented regurgitation. Blood pressure, respiration, and pancreatic secretion were recorded.

In control experiments, 5 mg. of histamine dichloride per kilo body weight was introduced into the duodenum. No change in blood pressure was ever produced. In another series of animals, we first introduced 5 to 10 cc. of chloroform, diluted with 1 to 2 volumes of paraffin oil. The chloroform usually caused a transient disturbance in the blood pressure. When recovery had occurred, and a steady level had been maintained for some time the histamine was administered. There was a prompt and prolonged fall of pressure, usually with a gradual recovery, the whole effect lasting 40 minutes to an hour or more.

Similar results were obtained when the following agents were used:

Hydrochloric acid, 0.4%, 20 to 40 cc. carbon tetrachloride, undiluted, 15 to 25 cc. Ethyl alcohol, 15 to 30% concentration, 20 to 30 cc. When alcohol was used, we substituted ether for barbital as the anesthetic.

Dog's gastric juice, of free acidity equivalent to 0.4% HCl, was also used, in amounts of 30 cc. The subsequent introduction of histamine caused only a slight fall of blood pressure, the gastric juice appearing to be less effective than simple water solution of HCl.

Sodium fluoride, in 1% solution, gave negative results. In stronger concentrations the fluoride itself produced a gradual fall of blood pressure, which was only slightly accelerated by the administration of histamine.

Some experiments were also carried out on the colon. When histamine was introduced alone, there was no effect on blood pressure. When it was preceded by alcohol or 0.4 HCl, it produced a marked fall. The other substances were not tried.

The respiratory effects were variable, and there was never a stimulation of pancreatic secretion.

Koessler and Hanke² found that histamine disappears from the normal dog's intestines at a rate which would be sufficient, if all passed unchanged into the circulation, to produce demonstrable effects. They conclude that it is "rendered pharmacologically inert in its passage through the intestinal wall." It seems possible that the influence of chloroform, alcohol or HCl may be to interfere with this detoxifying process, rather than directly to facilitate absorption.

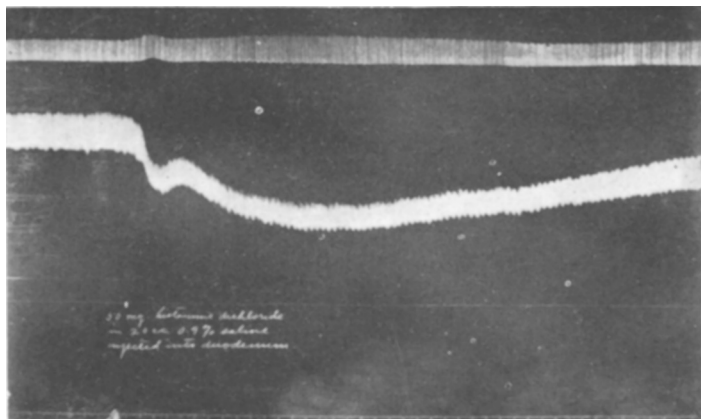


FIG. 1.

9 kilo dog, barbitol anesthesia. Showing the effect of 50 mg. histamine in the duodenum. 10 cc. of chloroform in 10 cc. paraffin oil had been introduced 48 minutes previously. Time tracing in minutes. Respiration (above) and carotid blood pressure (below).

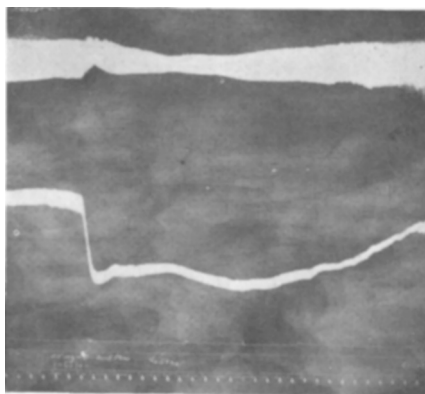


FIG. 2.

5.2 kilo dog, ether anesthesia. Effect of 55 mg. histamine (ergamine acid phosphate) in colon. 20 cc. of 30 per cent alcohol had been introduced 20 minutes previously. Respiration (above) and carotid blood pressure (below). Time, minutes.