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Effect of Rectally Administered Ether-Oil Mixtures on Absorption of Histamine from the Colon.

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Koessler and Hanke[1] showed that histamine and other amines are produced by bacterial activity in the intestine, and that histamine is apparently detoxified during absorption through the intestinal wall. Best and McHenry[2] have found in the intestinal mucosa of the dog an enzyme which destroys the physiological activity of histamine. It seems, therefore, that the process of detoxication may be an important function of the normal mucosa.

In an earlier paper from this laboratory[3] it was shown that exposure to certain chemical agents renders the dog's intestine permeable to histamine. Such an effect was noted with alcohol and chloroform, in varying dilutions. It therefore seemed of interest to study the effect of ether, because of the extensive use of ether-oil mixtures given per rectum for anesthesia.

Small dogs, in good health, were used. Preparation included 18 hours without food, 10 mg. per kilo of morphine sulphate given subcutaneously, and an enema of warm tap water. Anesthesia was induced by ether inhalation, which was lightened subsequently whenever additional ether was given per rectum. Records were made of respiration and of carotid blood pressure. A soft rubber catheter and draining tube were fixed in place for rectal injections. The dose of ether-olive oil mixture was 3 cc. per kilo body weight, as in the experiments of Beckmann, cited by Gwathmey.[4] The ratio by volume of ether to oil was varied from 75/25 to 35/65. After retention from 5 to 20 minutes the residue was washed out with saline solution. Five to 10 minutes later histamine dichloride (Eastman), 5 mg. per kilo in saline solution, was allowed to run into the colon.

Under these conditions, the administration of histamine was followed in every instance by an immediate and marked fall of arterial pressure. The general curve was similar to those shown in

[1] Koessler, K. K., and Hanke, M. T., *J. Biol. Chem.*, 1924, **59**, 889.

[2] Best, C. H., and McHenry, E. W., *Am. J. Physiol.*, 1930, **93**, 633.

[3] Mammoser, L. F., and Boyd, T. E., PROC. SOC. EXP. BIOL. AND MED., 1929, **26**, 765.

[4] Gwathmey, J. T., *J. Am. Med. Assn.*, 1929, **93**, 447.

the paper of Mammoser and Boyd.[3] The degree and duration of the depressor effect varied with the concentration of ether used. The maximum fall observed was from 128 to 76 mm., after retention of 75% ether for 5 minutes. In this instance the pressure after 48 minutes was still 12 mm. below the original level. The smallest fall recorded was from 126 to 112 mm., after retention of 35% ether for 20 minutes. The pressure remained below the original level for only 14 minutes.

In control experiments an enema of olive oil alone, or of saline, was substituted for the ether-oil mixture. Histamine subsequently administered did not affect the arterial pressure.

In all the concentrations used, therefore, ether appears to render the epithelium of the large bowel permeable, in some degree, to histamine. The normal impermeability, however, is largely or completely regained within 24 hours. Two dogs received the routine morphine injection and warm-water enema. A 65/35 ether-oil mixture was given by catheter and retained for one hour, the residue being washed out with saline. The dogs were allowed to recover, and 24 hours later were anesthetized by ether inhalation. The blood pressure was recorded and the usual dose of histamine given by catheter. In one dog the pressure was entirely unaffected, in the second there was a transitory fall of only 8 mm.

Some hyperemia was noted in the colon mucosa of 7 out of 8 dogs receiving ether and oil plus histamine. The mucosa in the control animals appeared normal, so the hyperemia was not due to histamine alone.

The amounts of histamine which we used were presumably larger than would ever exist under normal conditions at any one time in the bowel. In view of the marked depressor action, however, it seems probable that much smaller amounts would have produced effects of physiological importance. There is also a possibility that ether and similar agents may affect the absorption, or detoxication, of other potentially toxic substances besides histamine.