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Demonstration of the Humoral Agent in Fat Inhibition of Gastric Secretion.

T. KOSAKA AND R. K. S. LIM.

From the Department of Physiology, Peiping Union Medical College, Peiping.

Since the ingestion of fat results in the inhibition of the secretion of autotransplanted (*i. e.*, completely denervated) gastric pouches (Feng, Hou and Lim[1]), the mechanism concerned must be a humoral one. It was thought that as fat causes the ejection of bile into the duodenum, the reabsorbed bile (salts) might be the humoral agent, but this has been proved not to be the case (Kosaka and Lim[3]). The influence of fat on the gall bladder has been shown by Ivy and Oldberg[2] to be due also to a humoral agent. Having a sample of Ivy's gall bladder hormone, *viz.*, cystokinin, on hand, this was tried and found to inhibit gastric secretion in large doses (5 gm. per kg.). An attempt was therefore made to recover the gastric inhibitory agent from the intestine.

The upper small intestine of dogs (under ether or decerebrate) was ligatured in segments about 10 cm. long, and 50 cc. of olive oil introduced into alternate segments. After one hour, the intestine was removed and the mucosa exposed and unexposed to oil separately scraped off and extracted with N/10 HCl at a relatively low temperature (about 60°C.). Extracts have also been made simply with saline. Extracts from mucosa exposed to oil inhibit gastric secretion to a meat meal, when injected either intravenously or subcutaneously into Heidenhain-pouch dogs, the degree of inhibition produceable being comparable with that caused by the oral ingestion of fat (see Table I). Similar doses of the saline extract appear to have no effect on either the pancreatic or biliary secretion and do not depress the blood pressure. Further, when these extracts are heated to 80-100°C. for 10 minutes, the inhibitory effect is removed, and if HCl is added before heating, a gastric stimulating action is frequently obtained. Extracts from segments not exposed to oil exhibited no inhibitory action.

Extracts of the lower intestinal and colonic mucous membranes, which have been exposed to oil, are also inhibitory, while extracts of normal (*i. e.*, unexposed to oil) mucosa have no effect.

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[1] Feng, T. P., Hou, H. C., and Lim, R. K. S., *Chinese J. Physiol.*, 1929, iii, 371.

[2] Ivy, A. C., and Oldberg, E., *Am. J. Physiol.*, 1928, lxxxvi, 599.

[3] Kosaka, T., and Lim, R. K. S., *Chinese J. Physiol.*, 1930, iv, 213.

TABLE I.

The inhibition of gastric secretion by enterogastrone and other comparative data.

No. of Obs.	Basal secretion before feeding		Procedure (150 gm. meat, 100 cc. water)	Active secretion after feeding			
	2nd hr.	1st hr.		1st	2nd	3rd	4th
30	4.3	6.7	Control (standard meal)	32.4	21.8	11.9	7.3
22	1.4	2.7	Enterogastrone (from intestinal or colonic segments exposed to oil)	9.5	10.0	7.3	5.6
9	3.6	4.2	Control extract (from segments not exposed to oil)	48.5	16.0	10.9	7.0
8	1.0	1.5	Enterogastrone heated to 80°-100°C.	34.3	14.6	8.0	5.4
4	1.0	1.2	Olive oil into colon (40 cc.)	4.2	4.7	5.2	3.8
2	0.9	0.7	Other substances into colon	27.2	12.7	9.4	4.9
14	2.8	4.5	Olive oil *per os* (50 cc.)	4.8	16.4	17.6	10.4

Introduction of 40 cc. of olive oil into the colon at the same time as feeding meat, inhibits gastric secretion, while the introduction of other substances, *e. g.,* saline, gastric content, in large quantity fails to do so.

Extracts of gastric mucous membrane after exposure to oil have no inhibitory effect.

These observations show that an inhibitory agent may be formed in the mucosa of both the small and large intestine as the result of contact with fat, and provide further evidence in substantiation of the humoral theory of inhibition. The name Entero-gastrone (derived from *entero/n, gastr/on* and *chal/one*) is suggested for the gastric inhibitory agent.