Stimulation of Gastric Secretion by Commercial Cholecystokinin Extracts.* (31550)

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Previous investigators have shown that either a single injection of over 5 units per kilogram cholecystokinin (CCK) or injection of 0.5 unit/kg/min CCK inhibits gastric secretion(2). Recently we showed that injection of pancreatic juice or alkali into the duodenum increased gastric secretion, and injection of relatively small doses of secretin stimulated gastric secretion(7). Preshaw and Grossman have also found that small doses of secretin or CCK sometimes increase gastric secretion(5,6). The present paper is a study of the effects of CCK on gastric secretion in the dog.

Methods and results. Our whole experiment was carried out on ten 6- to 16-kg dogs equipped with Heidenhain pouches which had previously developed a secretory plateau during the third hour after feeding 200 g of proprietary dog food per hour (Fig. 1). A single intravenous injection of 1-5 units CCK‡/kg or continuous injection of 0.5 unit CCK/kg/min inhibited gastric secretion.

Experiments with food stimulation. A continuous infusion of 0.003 to 0.005 unit CCK/kg/min was given after a control period in 15 experiments on 5 dogs. There was an immediate, significant rise both in volume (13.3 ± 2.7 ml/hr to 22.3 ± 4.3 ml/hr) and in acid (2.04 ± .43 mEq/hr to 3.35 ± .71 mEq/hr) after the CCK was started ($p<0.01$). After the CCK was discontinued, the volume and acid returned to their previous levels (Fig. 2). The secretions for the fourth and fifth hours did not increase in 7 control experiments while in all 15 experiments where CCK was given there was an increase. Analyzing the data using Finney's 2 × 2 contingency table(1), the possibility that this occurred by chance is very slight ($p<.002$).

Fasting dogs. In a second set of 12 experiments on 4 fasting dogs, 0.003 to 0.005 unit CCK/kg/min produced a significant rise in both volume (0.8 ± 0.1 to 4.7 ± 0.6 ml/hr) and acid (0.004 to 0.23 mEq ± 0.005 mEq/hr) after the CCK was started, and a similar fall after the drug was discontinued ($p<0.01$).

Acetylcholine priming. After a priming dose of 0.2 μg acetylcholine per minute was given in 8 experiments on 5 dogs, the same dose of CCK as used before was given. Volume increased from 0.86 ± 0.06 mEq/hr to 3.1 ± 0.51, and the acid rose from 0.0 to 0.28 ± 0.06 mEq/hr. Both differences were significant ($p<0.01$) (Fig. 3).

Discussion. These experiments show that cholecystokinin (CCK) inhibits gastric secretion at only relatively high doses (over 0.5 unit/kg/min). Small doses of secretin or CCK stimulated rather than inhibited gastric secretion in our dogs in which pancreatic juice or alkaline material injected into the duodenum caused hypersecretion of the stomach(7). This suggests that CCK released when the duodenum is alkaline is responsible for the hypersecretion. Preshaw and Grossman(6) and Magee(4) used dogs in which the gastric secretory rate was high because of the diversion of pancreatic juice through an external pancreatic fistula.

The difference in CCK dosage between that required to inhibit and that to stimulate gastric secretion is about 100 times. Approximately 3 to 5 μg (5 units) per minute inhibit gastric output while 0.05 μg (0.05 unit) per minute stimulates secretion in a 10-kg dog. This could be compared with the gastric stimulation obtained by 0.05 μg of gastrin per minute in a 10-kg dog while 100 times this amount will inhibit gastric secretion. It appears to us that either there is some nonspecific secretagogue present in the mucosal

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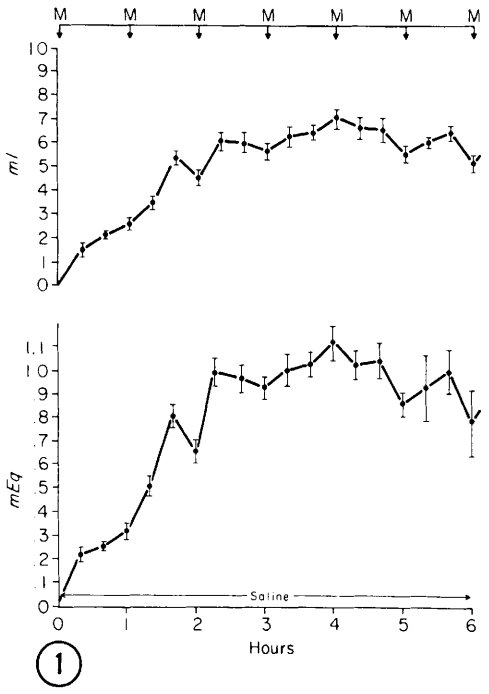
‡ Cecekin: Vitrum lot #214011 contains about 800 units CCK/mg. Another of CCK obtained from Professor Jorpes contains 1500 u/mg.



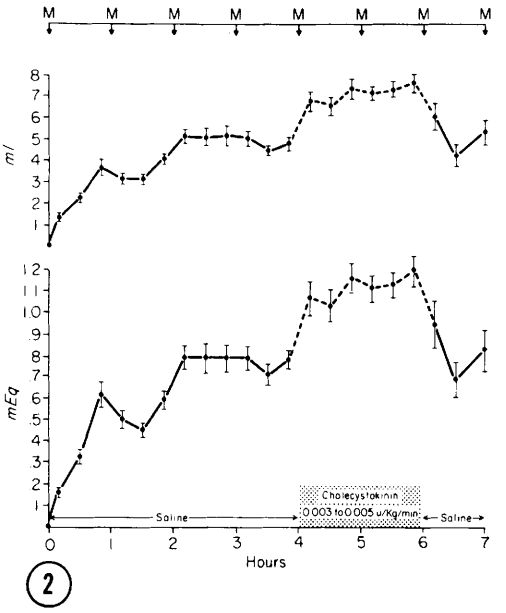


FIG. 1. Effect of feeding 200 g of proprietary dog food per hour. Mean and standard error of mean of 7 experiments on 4 dogs.

FIG. 2. Effect of 0.003-0.005 u/kg/min infusion CCK on food stimulated Heidenhain pouch secretion. Mean and standard error of mean of 15 experiments on 5 dogs.

extracts of the hog small intestinal mucosa said to contain 800-1500 units cholecystokinin per mg or that there is a minute quantity of gastrin in the mucosal extracts(3). It remains to be seen whether or not we are dealing with the same substance or impurities in two different substances.

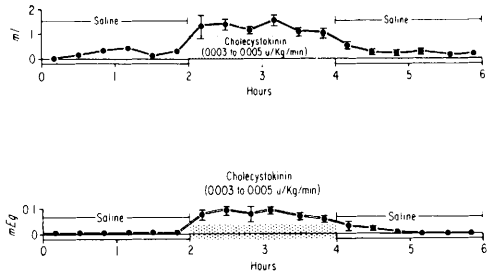


FIG. 3. Effect of 0.003-0.005 u/kg/min infusion CCK on dogs receiving 0.2 μg acetylcholine/min. Mean of 8 experiments on 5 dogs and standard deviations.

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