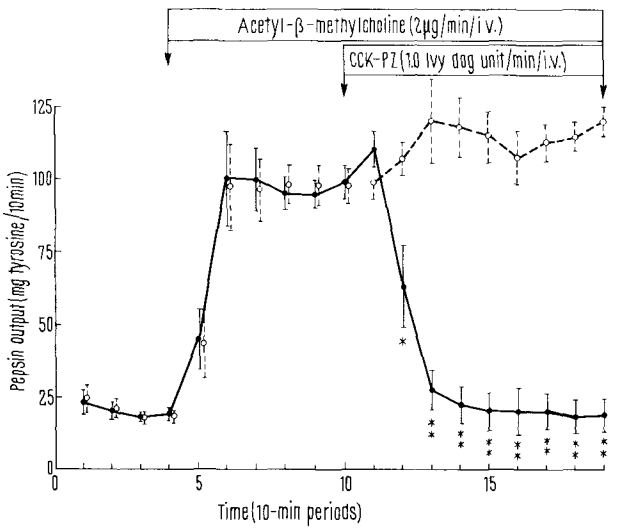
Inhibitory Action of Cholecystokinin-Pancreozymin on Gastric Pepsin Secretion

It has recently been demonstrated that secretin inhibits acid and stimulates pepsin secretion of the stomach[1,2]. Although another characterized duodenal hormone, cholecystokinin-pancreozymin (CCK-PZ) when administered alone has been shown to stimulate acid secretion[3,4], the action of this hormone on pepsin secretion is unknown. The present investigation was undertaken to determine the effect of CCK-PZ on pepsin secretion stimulated by acetyl-β-methylcholine (mecholyl), the cholinomimetic agent. There are no known physiological inhibitors of pepsin secretion.

Materials and methods. Six adult mongrel dogs of either sex, weighing from 16 to 20 kg, were first prepared with a vagally denervated Heidenhain pouch. After recovery from the operation, a duodenal pouch was constructed by transecting the bowel at the pyloric sphincter and just above the entrance of the main pancreatic duct. The common bile and accessory pancreatic ducts were ligated and transected. The gallbladder was anastomosed to the jejunum approximately 10 cm distal to the point where gastro-jejunostomy had been performed. The proximal end of the separated duodenal segment was closed and the distal end was brought out through the abdominal wall as a mucocutaneous fistula. The proximal end of the remaining duodenum was closed and gastrointestinal continuity was re-established by gastrojejunostomy. Thus the entry of gastric acid into the duodenum was prevented. Secretory studies were started two or more weeks following recovery from surgery. Before each experiment the animals were fasted, except for water, for a period of 18 h. A continuous i.v. infusion of 154 m*M* NaCl was delivered throughout each test at a rate of 60 ml/h. After the initial control of four 10 min collections, mecholyl (2 μg/min) was added to the saline infusion for the next 150 min. CCK-PZ (1.0 Ivy dog unit/min) was then added to the infusion 60 min after the start of mecholyl. Control experiments were performed in which mecholyl was administered by itself for the duration of the study on a given day. Before the start of the experiments the Heidenhain pouch was washed clean with saline and filled with 25 ml of saline. This was collected and the pouch was washed through with a further 25 ml of saline every 10 min as described previously[5]. The perfusate and the washout were combined and the volume of a sample was measured. The aliquot of each sample was immediately acidified to pH 2.0–2.5, if needed, by the addition of 0.01 ml of 16 *M* HCl and subsequently assayed for peptic activity by a NORTHROP's[6] modification of the hemoglobin substrate method of ANSON[7]. CCK-PZ (batches 26761 and 26841) used was provided by Professor J. E. JORPES of Chemistry Department, Karolinska Institutet, Stockholm (Sweden).



Effect of continuous i.v. infusion of cholecystokinin-pancreozymin (CCK-PZ) on Heidenhain pouch pepsin secretion stimulated by acetyl-β-methylcholine (mecholyl). ○------○, Control; ●——●, Mecholyl + CCK-PZ; *, $P < 0.02$; **, $P < 0.001$. Control received only mecholyl throughout the experiment. Each point represents the mean of 6 experiments in 6 dogs, the vertical bars indicate S.E. of the mean.

Results and discussion. CCK-PZ produced highly significant inhibition of gastric pepsin secretion stimulated by mecholyl (Figure). Inhibition was prompt, 41% within 10 min after the start of CCK-PZ administration, and 85% at the end of the administration. Our preliminary experiments also show that CCK-PZ in physiological doses significantly inhibits secretin-stimulated pepsin secretion from the Heidenhain pouch. KOSAKA and LIM[8] found that an extract of duodenal mucosa made after exposure to olive oil inhibited gastric acid and pepsin secretion and named the active principle enterogastrone. If enterogastrone exists physiologically as the specific hormone defined by KOSAKA and LIM[8], it has to be demonstrated to possess inhibitory actions on both acid and pepsin secretion. Secretin cannot be enterogastrone, because it has been shown to have stimulatory action on pepsin secretion. It is now well established that CCK-PZ significantly inhibits the acid response to gastrin extract[9], to the synthetic pentapeptide[3] and to endogenously released gastrin[10]. Since CCK-PZ is a potent inhibitor of pepsin secretion, it appears likely that CCK-PZ might be enterogastrone.

Zusammenfassung. Der Einfluss von Cholecystokinin-Pankreozymin auf die Sekretion von Pepsin wurde in Hunden mit Heidenhain-Tasche untersucht. Während submaximaler Pepsinstimulation mit Mecholyl verminderte i.v. Injektion von Cholecystokinin-Pankreozymin die Pepsin-Sekretion im Magen signifikant. Es wird vermutet, dass CCK-PZ Enterogastrone sein könnte.

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