The Effect of Glucagon on Brunner's Gland Secretion in Dogs (34386)

RAYFORD S. JONES AND ALBERT D. HALL
(Introduced by M. I. Grossman)
Surgical Service, Veterans Administration Hospital, San Francisco, California 94121; and Department of Surgery, University of California School of Medicine, San Francisco, California 94122

Glucagon, a polypeptide containing 29 amino acid residues with a molecular weight of 3482 (1), affects the gastrointestinal tract by inhibiting gastric motility (2), inhibiting intestinal motility (3), inhibiting gastric acid secretion (4), inhibiting pancreatic secretion (5), and stimulating hepatic bile flow (6). Stening and Grossman (7) have recently shown that secretin stimulated Brunner's gland secretion in dogs and cats. Because secretin and glucagon are similar in structure (1, 8) and share several actions upon the gastrointestinal tract, the following experiment was performed to determine if glucagon also stimulated secretion from duodenal pouches.

Methods. Proximal duodenal pouches were prepared in 3 mongrel dogs weighing 14.5 to 18.2 kg by constructing a double mucosal septum at the pylorus and transecting the duodenum proximal to the junction of the common bile duct with the duodenum. The proximal end of the divided duodenum was brought through an abdominal stab wound and sutured to the skin as mucous fistula draining the duodenal pouch. The distal portion of the cut duodenum was used to reestablish gastrointestinal continuity with a side to end gastroduodenostomy. Experiments were begun no sooner than 3 weeks after surgery. After an 18-hr fast, the dogs were placed in sling harnesses and an intravenous infusion was started through a polyethylene tube (PE 50) in a leg vein. The infusion was maintained at 66 ml/hr with a calibrated peristaltic pump (Harvard Apparatus Company, Millis, Mass.). After infusing 0.15 *M* NaCl solution for four 15-min periods, glucagon (Lilly) dissolved in 0.15 *M* NaCl was infused for eight 15-min periods, then 0.15 *M* NaCl alone was given for the remaining four 15-min periods of the 4-hr experiments. Glucagon was given in doses of 2, 4, 8, 16, 32, 64, and 128 μg/kg-hr. Only a single dose of glucagon was given during any experiment. Control experiments were performed similarly by giving glucagon diluent in 0.15 *M* NaCl instead of glucagon as described above. To determine the effect of hyperglycemia upon Brunner's gland secretion, glucose instead of glucagon was infused for eight 15-min periods. Other experiments were performed by giving each of the dogs 100 ml of 50% glucose orally. The secretion from the Brunner's gland pouches was collected via a plastic funnel strapped to the dog's abdomen about the opening of the pouch. The volume of secretion was measured to the nearest 0.1 ml.

Results. The continuous intravenous infusion of glucagon resulted in a prompt and sustained increase in the volume of secretion from the Brunner's gland pouches with elevations of secretion occurring in the first 15-min period of stimulation. The responses to 4, 16, and 64 μg/kg-hr are shown in Fig. 1. The dose–response relationships of glucagon and Brunner's gland secretion are shown in Fig. 2. The response to each dose was taken as the mean of the volumes of the eight 15-min periods during glucagon infusion. Control values were obtained similarly during infusion of glucagon diluent. The lowest dose of glucagon producing a significant increase, 8 μg/kg-hr, gave 0.7 ml/15 min; this was significantly greater than control secretion, 0.3 ml/15 min.

The responses to 8, 16, 32, and 64 μg/kg-hr glucagon were plotted against the logarithm

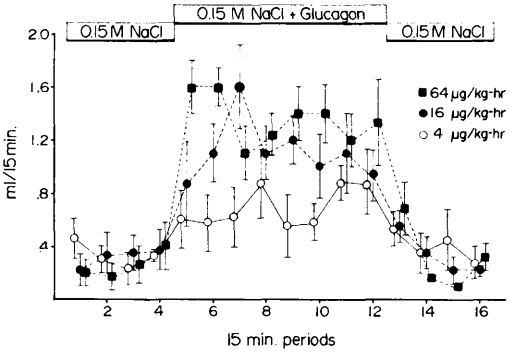

FIG. 1. The effect of glucagon infusion on Brunner's gland secretion. Each point represents the mean of 2 experiments on each of 3 dogs. In Figs. 1–5, vertical lines indicate the SEM.

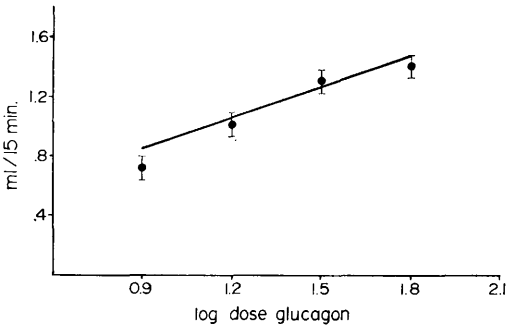

FIG. 3. Relationship between the logarithm of glucagon dose and volume of Brunner's gland secretion. Each point represents the mean of 2 experiments on each of 3 dogs.

of the doses (Fig. 3). This line was calculated by the method of least squares and the dose response relationship was linear and responses were dependent upon log dose ($p<0.025$) (9).

The effect of glucose upon Brunner's gland secretion is shown in Fig. 4. The infusion of 0.28 and 0.55 *M* glucose at 66 ml/hr produced no increase in the volume of Brunner's gland secretion. The average blood sugar of the 3 dogs after 1 hr of glucose infusion was 98 mg/100 ml for 0.28 M and 160.7 mg/ml 0.55 *M* infusions, respectively. The oral administration of glucose had no effect on Brunner's gland secretion (Fig. 5).

Discussion. In 1935 Florey and Harding (10), using transplanted duodenal pouches, showed that Brunner's gland secretion was controlled by a humoral mechanism. The identity of the hormone or hormones responsible for the stimulation of Brunner's gland secretion has been in question (11–14) until recently when Stening and Grossman (7) demonstrated clearly that natural porcine secretin as well as synthetic secretin stimulated Brunner's gland secretion in dogs and cats. The latter authors also showed that cholecystokinin and caerulein produced increased secretion from Brunner's glands.

Glucagon and secretin are similar in structure (1, 8) and share certain actions upon the gastrointestinal tract such as inhibition of gastric acid secretion (4, 15), inhibition of gastric motility (2, 16) and stimulation of hepatic bile flow (6, 17). The data of the present experiment indicate that stimulation of Brunner's gland secretion is another gastrointestinal action of glucagon. The role of

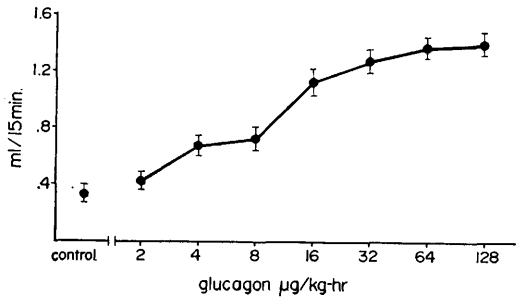

FIG. 2. The dose response relationship between glucagon infusion and volume of Brunner's gland secretion. Each point represents the mean of 2 experiments on each of 3 dogs.

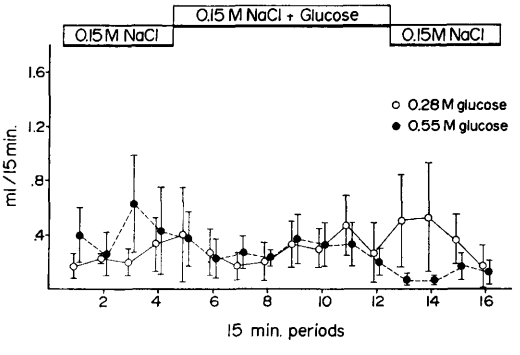

FIG. 4. The effect of glucose infusion on Brunner's gland secretion. Each point represents the mean of 1 experiment on each of 3 dogs.

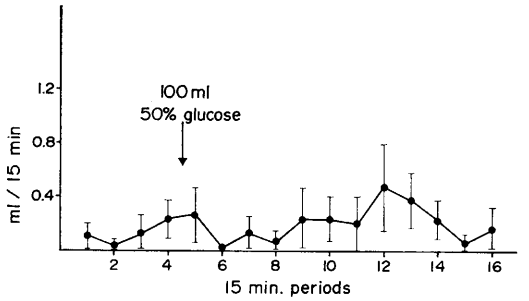

FIG. 5. The effect of orally administered glucose on Brunner's gland secretion. Each point represents the mean of 1 experiment on each of 3 dogs.

endogenous glucagon as a physiologic stimulant of Brunner's gland secretion cannot be assessed from this experiment. Unger (18) showed that intraduodenal administration of glucose caused increased glucagon-like immunoreactivity in vena caval plasma of dogs. The failure of orally administered glucose to stimulate Brunner's glands suggests that intestinal glucagon-like substance is not a stimulant of duodenal secretion.

Summary. Pouches were prepared from the proximal duodenum in mongrel dogs and intravenous infusion of glucagon caused dose related increases in the volume of secretion from these pouches. The maximal response, 1.4 ml/15 min, was produced by a glucagon dose of 64 μg/kg-hr. Glucose infusions did not stimulate Brunner's gland secretion, indicating that the hyperglycemic effect of the glucagon was not responsible for the increase in duodenal secretion. Oral glucose administration also failed to stimulate Brunner's gland secretion.

This work was supported by a Veterans Administration Clinical Investigator appointment (R.S.J.). The authors gratefully acknowledge the technical assistance of Elizabeth Stevenson. Dr. K. Jan Bossart kindly assisted in the surgical preparation of the animals used in this study. A portion of the glucagon used in this experiment was supplied by the Eli Lilly Company.

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Received July 22, 1969. P.S.E.B.M., 1969, Vol. 132.