Effect of long-term parenteral feeding on gastric secretion in dogs

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THOR, PIOTR J., EDWARD M. COPELAND, STANLEY J. DUDRICK, AND LEONARD R. JOHNSON. Effect of long-term parenteral feeding on gastric secretion in dogs. Am. J. Physiol. 233(1): E39-E43, 1977 or Am. J. Physiol.: Endocrinol. Metab. Gastrointest. Physiol. 1(1): E39-E43, 1977. Three dogs were surgically prepared with gastric fistulas and Heidenhain (vagally denervated) pouches. Acid and pepsin responses to pentagastrin and food were determined before, at the end of a 1-wk period of total parenteral feeding, and 1 mo after the resumption of a normal oral diet. Acid and pepsin output from the denervated pouch in response to pentagastrin and food decreased significantly (P < 0.001) after parenteral feeding and returned to control levels after the dogs resumed a normal diet. Secretory outputs from the gastric fistula in response to pentagastrin remained unchanged throughout the experiment. Basal serum gastrin levels decreased 50% during the period of intravenous feeding and returned to levels approximately twice the control levels following resumption of normal oral food intake. Serum gastrin responses to a meal also decreased during intravenous alimentation and returned to higher than normal levels following a 1-mo period of oral intake. These studies indicate that the absence of oral food intake in the dog does not result in decreased acid secretion from the innervated stomach. Vagal innervation in some way is responsible for the preservation of normal secretion during the absence of food from the gastrointestinal tract of the dog.

Parenteral nutrition; acid; pepsin; gastrin

Parenteral nutrition has become a widely used clinical technique since its description in 1968 (5). One benefit of this procedure is the reduction of drainage from high enteroenterostomy fistulas and subsequent fistula closure (4). The mechanism involved in this decreased fluid output is presumed to be decreased gastric and pancreatic secretion due to the lack of normal stimuli created by the ingestion and presence of food within the gastrointestinal tract. Whether the long-term absence of oral food intake results in decreased secretory capacities has not been investigated.

Our laboratory has used total parenteral nutrition as a tool to study the effects of food on the gut. In the rat, a 2-wk absence of oral food ingestion results in significant decreases in the weights of the oxyntic gland area of the stomach, small intestine, and pancreas. Disaccharidase levels drop significantly, and antral and serum gastrin levels are considerably lower (8). The changes in tissue weights and enzyme activity are largely prevented by the addition of a low dose of pentagastrin to the intravenous nutrient solution (9). This is the first study which examines gastric secretion following the long-term absence of food from the gut.

Methods

Experiments were performed on three male dogs weighing 15-19 kg. Each dog was anesthetized with thiopental sodium, 20 mg/kg, and methoxyflurane. A laparotomy was performed under aseptic conditions and a vagally denervated pouch (Heidenhain type) was constructed from the oxyntic gland area of the stomach. The pouch was drained to the outside through a Gregory cannula. A gastric fistula was created by inserting a Thomas cannula in the most dependent portion of the gastric remnant.

The animals were supported by slings and trained to stand quietly on tables. Experiments began 3 wk following surgery. A peripheral leg vein was cannulated and saline infused via a Harvard peristaltic pump at a rate of 1 ml/min. The gastric fistula was opened and both the main stomach and denervated pouch were washed gently with distilled water and allowed to drain. Basal secretion from both the Heidenhain pouch and gastric fistula was collected for two 15-min periods.

Two types of studies were performed. In one series, pentagastrin (Imperial Chemical Industries) was infused in doses increasing in a stepwise manner of 0.5, 1.0, 2.0, and 4.0 μg/kg per h. Each dose was infused for three 15-min collection periods. In the other study, one can of dog food (Prescription Diet Riviano Foods, Hill’s Division, Topeka, Kans.) was fed following the collection of basal secretion. Gastric juice was collected at 15-min intervals for 3 h following feeding. The food was entirely consumed in each instance within a few minutes of presentation. Blood samples for serum gastrin assays were collected at the end of the basal period and at 30 and 60 min following eating. Two experiments of each type were run on each of the three dogs, so all mean values reported are from six observations.

The volume of each secretory sample was measured
and aliquots were taken for determination of acid and pepsin concentrations. Acid content was determined by titration with 0.2 N NaOH to pH 7.0 using an automatic titrator and pH meter (Autoburette, Radiometer, Copenhagen, Denmark). Pepsin concentrations were measured using a modification (11) of the Anson (1) hemoglobin method and were expressed as milligrams pepsin per milliliter by reading the trichloroacetic acid supernatant at 280 nm and comparing it with solutions incubated with different amounts of pepsin standard (hog pepsin, Pentex Biochemicals). Pepsin outputs were calculated and expressed as milligrams pepsin per 15 min. Results for the pentagastrin studies were expressed as acid and pepsin outputs for the last 30 min of infusion of each dose. For the feeding studies, two consecutive 15-min periods were combined and outputs were expressed per 30 min. Serum was collected from each of the 5-ml blood samples and frozen for gastrin radioimmunoassay. The gastrin assays were done in one batch at the end of the entire study according to the method described by Yalow and Berson (15) and using an antibody characterized by Dockray and Walsh (3). Synthetic human gastrin I, 1-17, obtained from Imperial Chemical Industries, Ltd., England, was used as a standard. Gastrin levels are expressed as picograms of G-17 equivalents per milliliter serum. Experiments were carried out on alternate days and not more frequently than 3 times per week. The order of experiments was randomly assigned.

Following the completion of both studies, an intravenous catheter was inserted through a superficial neck vein and advanced into the vena cava. The dogs were placed in metabolic cages and the catheter was inserted through a swivel apparatus, Harvard peristaltic pump, and connected to a reservoir containing the intravenous nutrient solution. This arrangement allowed for complete mobility of the dogs within the cages without twisting or cramping the catheter (5).

Infusion of the alimentation solution began immediately and was gradually increased to 1,200 ml/day. The nutrient solution consisted of 4.25% Freemail (solution of essential free amino acids) and 25% dextrose. Salts were added so that each liter contained 50 meq NaCl, 50 meq Na acetate, 40 meq K acetate, 15 meq K.HPO4, 15 meq NaSO4, and 1 g Ca gluconate. Solutions were passed through a 0.22-μm membrane filter. The animals were fed totally by vein for 1 mo during which they gained from 0.8 to 1.7 kg body wt and appeared to be in excellent health. Both series of secretory tests were then repeated as described previously. During testing the intravenous alimentation catheter was kept open by a saline drip.

Following the completion of the second series of secretory tests, the animals were returned to a conventional diet of Purina dog chow. Secretory testing was repeated 1 mo later.

The period of total intravenous alimentation had no discernible effect on the dogs' appetites. Each animal immediately consumed the entire test meal when presented. The animals also ate well when switched back to normal oral food intake. There were no instances of vomiting, diarrhea, or other evidence of intolerance.

The weights of the animals remained relatively constant following resumption of oral food intake.

Secretory data are expressed as means and standard errors of the means of two observations in each of the three dogs, so that n = 6 for each value. The means of two gastrin values were obtained for each dog at each time interval for each of the three series of studies and are shown in Table 1. Means and standard errors of the means were calculated for n = 3. Significance was assessed with the Student t test for unpaired values. Differences were considered significant if P < 0.05.

**RESULTS**

Following 1 mo of total parenteral feeding, both Heidenhain pouch acid (Fig. 1) and pepsin (Fig. 2) responses to a meal decreased precipitously. At all time intervals following feeding, acid and pepsin outputs were significantly lower (P < 0.001). Both responses had returned to normal 1 mo after the resumption of normal oral food intake (Figs. 1 and 2). Heidenhain pouch acid and pepsin outputs in response to pentagastrin also declined significantly after the absence of food from the gut for 1 mo (Figs. 3 and 4). Although the decreased response to pentagastrin was not as great as it was to a meal, outputs were significantly lower at each dose of pentagastrin (P < 0.05). Both acid and pepsin outputs in response to pentagastrin had returned to control levels 1 mo after the resumption of normal oral food intake (Figs. 3 and 4).

The absence of food from the gastrointestinal tract did not alter either acid (Fig. 5) or pepsin (Fig. 6) output from the vagally innervated stomach in response to pentagastrin.

Basal serum gastrin levels decreased approximately 50% during the period of total parenteral feeding and returned to normal levels after the animals were placed back on oral diets (Table 1). Serum gastrin increased 30 and 60 min after a meal regardless of the diet regimen. Absolute gastrin levels 60 min after eating were significantly lower following the 1 mo absence of food from the gut. The percent increase in serum gastrin over basal levels, however, was actually higher at this time, indicating that the absence of receptor stimulation for the release of gastrin during the period of parenteral nutrition did not impair the gastrin release mechanism. Gastrin outputs in response to a meal were significantly

**TABLE 1. Serum gastrin before, 30, and 60 min after a meal**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Before Parenteral Feeding</th>
<th>After Parenteral Feeding for 1 mo</th>
<th>Normal Oral Diet For 1 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Basal 30 min 60 min</td>
<td>Basal 30 min 60 min</td>
<td>Basal 30 min 60 min</td>
</tr>
<tr>
<td>A</td>
<td>101 228 410</td>
<td>46 126 169</td>
<td>55 194 254</td>
</tr>
<tr>
<td>B</td>
<td>122 320 357</td>
<td>59 207 267</td>
<td>151 430 630</td>
</tr>
<tr>
<td>C</td>
<td>103 210 310</td>
<td>71 223 180</td>
<td>190 406 577</td>
</tr>
<tr>
<td>X</td>
<td>109 244 398</td>
<td>59 185 292</td>
<td>120 344 487</td>
</tr>
<tr>
<td>SEM</td>
<td>6.7 4.1 2.3</td>
<td>7.2 3.0 3.3</td>
<td>4.2 7.5 11.8</td>
</tr>
</tbody>
</table>

Values are in picograms per milliliter. Experiments were done before 1 mo after the start of total parenteral feeding, and 1 mo following return to normal oral food intake. *P < 0.001. † P < 0.005. ‡ P < 0.05. § P < 0.02.
higher than control levels after the dogs had been feeding normally for 1 mo (Table 1)

DISCUSSION

This is the first study to examine the effects of the long-term absence of food from the gut on gastric secretion. There have been several studies from the surgical literature concerning the mechanism by which total
repoerted to the intravenous nutrient solution pre- 
vented most gastrointestinal tract weight loss as well as 
the decreases in disaccharidase activity which occur in 
these animals (2, 9). On the basis of the rat data one 
might have expected canine gastric secretion in re-
spnse to pentagastrin to be decreased because of de-
creased mass of secretory mucosa and the response to a 
meal to be decreased for the same reason and because of 
lower endogenous gastrin levels. This clearly was not 
the case for the vagally innervated stomach. 

Even though basal serum gastrin levels decreased 
50% as a result of parenteral feeding, the serum gastrin 
response to the meal was unchanged at 30 min and only 
slightly lower than control levels 60 min after feeding. 
In fact, the percentage change in serum gastrin level in 
response to a meal was greater following the period of 
intravenous feeding than it was during the control pe-
riod 1 mo earlier The fact that both acid and pepsin 
outputs from the main stomach were unchanged during 
the course of the experiment indicates that neither the 
parietal cell mass nor the sensitivity of the parietal cells 
to gastrin changed during the prolonged absence of food 
from the stomach. 

Acid and pepsin output from the vagally denervated 
Heidenhain pouch, however, decreased significantly in 
response to both pentagastrin and food. The calculated 
maximal output of the Heidenhain pouch in response to 
pentagastrin decreased from the control value of 1.163 
meq H+ /30 min to 0.683 meq H+/30 min after 1 mo of 
intravenous feeding. During the same period the Ks or 
D50 for acid secretion increased from 1.37 to 2.62. These 
changes imply that both the secretory mass (or individual 
parietal cell response) and parietal cell sensitivity to 
pentagastrin decreased during this period of time. This
accounts for the large decrease in acid secretion. That these changes were not permanent is evidenced by the total recovery of secretory capacity after the animals resumed normal oral feeding. The pouch response to food was depressed even more than the response to pentagastrin. The factors, mentioned above, responsible for the decrease to pentagastrin stimulation are, in part, responsible for the decreased secretion in response to a meal. To these must be added the significantly decreased serum gastrin response which was evident 60 min after eating.

This is the first study examining the effects of long-term absence of an oral food intake on the dog stomach. Numerous species differences are evident when compared to the rat. After 10 days of parenteral nutrition, rat serum gastrin decreased to one-eighth control levels (9) compared to one-half in the current study. Food deprivation for a period of 4 days in the rat resulted in a drop in serum gastrin levels to one-seventh the normal level (1). Thus, maintenance of rat gastrin levels seems to depend on stimuli for gastrin release. While there was some evidence of this in the current experiments on the dog, the dependence is not nearly as great. In the rat, decreasing endogenous gastrin levels by any means results in hypoplasia of gastrointestinal tract tissues dependent on the trophic hormone (7). Gastrin is also a trophic hormone for the dog oxyntic gland mucosa (13), and there appears to be no difference between the trophic responses in the two species. Therefore, since acid secretion did not change, one must conclude in the current studies that either endogenous gastrin levels did not drop sufficiently to cause atrophy of the inner-

REFERENCES