Effect of diet on gastric secretion\textsuperscript{1,2}

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ABSTRACT Meals stimulate gastric acid secretion in man and animals. The lowest pH of gastric content in man, however, occurs during the early morning hours. Protein meals are both effective buffers raising the gastric pH immediately after ingestion and potent stimulants to acid secretion lowering the pH as the meal is emptied. Two methods, intragastric titration and marker dilution methods are available for measuring acid output in man to a meal. Acid secretion is influenced by the appetizing qualities and the chemical and physical characteristics of the meal. In man and cat acid secretion in response to a meal can equal the maximal response to histamine and pentagastrin. In the dog, it exceeds it. Fat delays the acid secretory response. Both the vagus nerves and gastrin are implicated in mediating the response. \textit{Am J Clin Nutr} 1985;42:1006-1019.

KEY WORDS Gastric acid secretion, meals, food

Introduction

The effect of food on secretion by the stomach is a matter of major interest to physiologists. Food intake is the strongest physiological stimulus to the secretion of acid and probably also of pepsinogens by the stomach. It is also a potent stimulus for the endocrine secretion of the peptide gastrin, the most potent known gastric secretagogue.

Until recently, there was no satisfactory method for the quantitative measurement of acid secretion in response to a meal in human subjects. Information was limited to changes in gastric intraluminal pH, mostly in patients with duodenal ulcer. Figure 1 shows the results of hourly determinations of pH in 12 subjects with duodenal ulcers over a 24-h period while taking three different diets: a bland diet, a limited convalescent diet, or a free choice of diet (1). The latter tended to lead to lower pH's, but the differences were not significant. Note the rise in pH (fall in [H\textsuperscript{+}]) after meals due to the buffering activity of the food. The lowest pH values occurred during the early morning hours.

Figure 2 shows the effect of the number of calories and the frequency of feedings on the intragastric pH over a 24-h period in 12 patients with duodenal ulcer (2). Note that higher caloric meals lead to both lower and higher pH values before and after meals respectively.

Frequent small feedings reduced the extremes of shifts in pH.

Figure 3 shows a comparison of equivalent caloric feedings of high carbohydrate with high protein diets in 14 patients with duodenal ulcers (3). Again, high protein diets lead to higher hydrogen ion concentrations before meals and lower values after meals. From these studies we can conclude that in patients with duodenal ulcers, appetizing diets, high in calories and protein content, are both better buffers of gastric HCl and more powerful stimulants of acid secretion. Frequent small feedings reduce the variability in gastric pH, but the lowest pH occurs during the early morning hours of the interdigestive or fasting period.

Within the last decade, two methods have been developed to permit measurement of acid output in human subjects in response to a meal. The first is that of intragastric titration. In brief, a protein or peptide-containing meal is taken and the amount of alkali required to be added to the stomach in order to maintain a pH of about 5.5 is taken as a measure of acid output. Figure 4 is an example of such a measurement.

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FIG 1. Mean pH of gastric content at different times of day in 12 patients with duodenal ulcer on three different diets, from Lennard-Jones and Babouris, 1965.

FIG 2. Mean pH of gastric content at different times of day and in response to different amounts of foods and different frequencies of meals in 12 patients with duodenal ulcer, from Babouris et al, 1965.
FIG 3. Mean pH of gastric content after diets high in carbohydrate or protein at different times of day in 14 patients with duodenal ulcer, from Lennard-Jones et al., 1968.

Study after a steak meal in six normal subjects and seven patients with duodenal ulcers (4). Note that the patients with duodenal ulcer secreted more acid than did the normal subjects. The major drawback of this method is that the pH is artificially pegged at 5.5, whereas under normal conditions it would fall to around 2.

The second method is based on marker-dilution methods in both the stomach and duodenum. Figure 5 shows the changes in pH after a liquid-solid meal in 6 normal subjects compared with the same meal after homogenization (5). Note that the pH is lower and the titratable acidity greater in both concentration and amount in gastric content without homogenization. Figure 6 shows the titratable acid output, pepsin output, and secretory volume after the two meals (5). Note the much greater response to the liquid–solid meal. Comparison of these results with maximal acid outputs after stimulation with pentagastrin or histamine indicate that meals are capable of stimulating maximal acid outputs.

Figure 7 shows the relative potency of various beverages in stimulating acid secretion in
Acid secretion are less well understood. There is an effect of intravenous nutrient solutions, such as those used in total parenteral nutrition (TPN). Figure 8 shows influence of two different rates of delivery of TPN solutions on basal output of acid compared to infusions of saline in 11 subjects during treatment with TPN. Note the greater acid outputs during TPN (7). On the other hand, maximal acid outputs were unchanged. These results indicate that absorbed nutrients can contribute to the acid response to a meal.

An appetizing meal can stimulate acid secretion during sham-feeding to a greater degree than routine institutional food (Fig 9) (8). In six normal subjects as determined by intragastric titration (6). Milk was the most potent stimulant exceeding the maximal acid output in response to pentagastrin (27.0 + 6.1 mM of HCl/h). Water stimulated acid output to about 40% of the pentagastrin-stimulated output, reflecting the effect of distention.

These results establish the importance of the size, chemical composition, and physical character of meals in determining the magnitude of the increase in gastric acid secretion.

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FIG 7. Mean maximum acid output (MAO) determined by intragastric titration in 6 normal subjects to nine beverages tested compared to water expressed as a percent of the MAO to pentagastrin. The mean response to pentagastrin was 27.0 ± 6.1 mM mol/h * = p < 0.05 compared to water control, and ** = p < 0.005, from Mc Arthur et al, 1982.

FIG 8. Effects of intravenous infusion of saline or two different rates of total parenteral nutritional solutions in 11 subjects on TPN. There were no differences in the response to pentagastrin, from Levine et al, 1980.
AVERAGE ACID RESPONSE TO SHAM FEEDING IN GASTRIC FISTULA SUBJECT

Collection Periods (15-minute intervals)


FIG 10. Gastric acid outputs to a peptone meal of varying pH determined by intragastric titration in six tests on each of six patients with duodenal ulcer, from Konturek et al., 1974.
The feeding of the food never enters the stomach. The stimulation is mediated through increased activity in the efferent or motor fibers of the vagus nerves. In this experiment the patient had an esophagostomy because of a lye stricture of the esophagus. Gastric acid secretion was collected from a gastrostomy.

Feeding also elicits inhibitory influences on gastric acid secretion. Figure 10 shows that the potency of a peptone meal in stimulating gastric acid secretion is reduced by lowering the pH of the peptone solution in six patients with duodenal ulcer (9). It is also known that lowering the gastric pH reduces the release of the acid secretagogue hormone gastrin into the blood stream.

The level of immunoreactive gastrin in the peripheral blood rises after a meal, as shown in Figure 11, in human subjects (10). The anticholinergic drug, atropine, which inhibits the secretion of vagally or acetylcholine-stimulated acid secretion actually increased the blood concentrations of gastrin. Figure 12 shows that there is a good linear correlation between the integrated gastrin output into the blood and the acid output in response to a meal in 19 normal subjects (11). These results indicate that although both vagal activity and gastrin release participate in the stimulation of acid secretion in response to a meal, the exact relationship between the two is complex.

For more specific details of the response of gastric acid secretion to a meal, experiments in animals offer advantages. Dogs equipped with vagally-innervated pouches of the acid-secreting mucosa make it possible to examine the acid secretion free of saliva, duodenal content, and alkaline antral (pyloric) secretions.
Increasing the weight of meat meals produced a dose-related increase in acid output from the pouch in three dogs as shown in Figure 13 (12). The maximal acid output to a meal exceeded that to gastrin by 30–60%.

Figure 14 shows the potency of various ingredients of the diet, such as beef, fish, poultry, fruit, and milk on acid secretion from six dogs with a similar pouch (13). Figure 15 shows results with purified foods in five dogs (14). These results show that protein-rich foods are the most potent stimulants to acid secretion. This correlates with their buffering capacity. The role of vagal innervation can be dem-
FIG 14. Mean acid outputs to an equivalent caloric amount of a variety of foods, as a percent of the response to meat in six dogs with vagally-innervated gastric pouches, from Saint-Hilaire et al, 1960.

FIG 15. Acid output from vagally-innervated gastric pouches in five dogs fed purified food substances as a percent of the caloric equivalent of 100 calories of meat, from Kotrba et al, 1969. Note that olive oil and the inert substance methylcellulose have nearly the same effect.

TEST MEALS
1 Lean Beef
2 Lactalbumen
3 Gluton
4 Casein
5 Gelatin
6 Egg Albumen
7 Olive Oil
8 Sucrose
9 Methylcellulose
FIG 16. Acid output from vagally-innervated (left) and denervated pouches (right) in the same six dogs, after stimulation by a meal of liver, heart, and bone meal, from Guldvog and Getz, 1981.

Demonstrated by comparing the response of a vagally-innervated pouch and a vagally denervated pouch in the same dog as shown in Figure 16 (15). Note that the response is markedly reduced by vagal denervation. However, the vagally-denervated pouch is even more sensitive to inhibition by an anticholinergic drug than the innervated pouch.

FIG 17. The effect of various doses of atropine sulfate on the serum gastrin increment above basal concentrations in response to a meal of boiled beef liver in seven dogs. The atropine was given 20 min before feeding. 0 = no atropine given, from Impicciatore et al, 1977.
The conflicting role of the cholinergic innervation in gastric release is shown by the dose response of gastrin release in response to testing with food or in response to an ingested meal to various doses of atropine. In Figure 17 doses of 12.5 to 25 μg/kg of atropine increased immunoreactive gastrin levels while those >50 decreased them in 7 dogs (16). On the other hand, Figure 18 shows that doses of 2-16 μg/kg reduced gastrin concentrations in 7 dogs where the meal was given directly into the gastric fistula (17). The possible explanations include a cholinergic inhibitory influence on gastrin release and/or vagally mediated release of bombesin-like peptide which then stimulates gastrin release. Cholinergic inhibition of somatostatin release has also been demonstrated.

These results indicate that both gastrin and vagal activity participate in exciting acid secretion in response to a meal. The heterogeneous nature of gastrins in the blood and the simultaneous release of other known and unknown regulatory peptides make it difficult to construct a suitable model to permit full understanding of the mechanism of the response.

Once the meal enters the duodenum, inhibitory influences on gastric acid secretion come into play. One of the most important of these is the inhibitory effect of fat in the small intestine on acid secretion. Figure 19 shows the effect of introducing fats into the stomach or

**FIG 18.** Gastrin release into the peripheral stimulated by a meat given into the gastric fistula of four dogs with intact vagus nerves. Either saline or atropine in varying doses was given intravenously. In separate experiments teasing with food was used as a cephalic stimulus. The data shown are the mean of gastrin above fasting levels, from Hirschowitz et al, 1981.
duodenum on the secretory response of vagally-innervated fundic pouch to a meat meal in a single dog (18). It can be seen that the acid secretory response is much delayed. Current research implicates the release of neurotensin in mediating this response. Cutting the vagi reduces the inhibitory effect of fat.

To summarize the effect of different food stuffs: proteins are the strongest stimulants and the most effective buffers. Fat has inhibitory or delaying effects on the acid response to a meal.

The cat, like human subjects, responds to a meal with a maximal acid secretion compared to pentagastrin, as shown in Figure 20 (19). As shown earlier in man, after sham-feeding, there is a good correlation in cats with vagally denervated pouches between the acid secretory response to a meal and the level of plasma immunoreactive gastrin (Fig 21) (20). The ad-
FIG 20. Acid output to a meat meal in nine cats with vagally-innervated gastric pouches compared to the response of a maximally stimulating dose of pentagastrin, from Svensson and Emas, 1979.

FIG 21. Relationship between acid output after meat feedings expressed as the percent of the peak acid output to feeding in eight cats with vagally-denervated gastric pouches and the serum gastrin as a percent of the maximum concentration reached after feeding. The relationship is unchanged by atropine, from Svensson et al, 1976.
ministration of atropine does not alter this relationship, but only a single dose of atropine was given.

**Conclusions**

The relative potency of food and beverages in stimulating acid secretion in response to meals has been identified in human subjects and animals. The mechanisms by which foodstuffs exert their effects are still controversial. Effects on gastric emptying must also be considered since the duration of the buffering capacity of protein in the stomach depends upon the rate of emptying.

**References**