Different Gastric, Pancreatic, and Biliary Responses to Solid-Liquid or Homogenized Meals

JUAN-R. MALAGELADA, MD, VAY L.W. GO, MD, and W.H.J. SUMMERSKILL, MD

We have compared responses to an ordinary solid-liquid (S) meal and to a homogenized (H) meal of identical composition (sirloin steak, bread, butter, ice cream with chocolate syrup, and water) by measuring simultaneously postprandial gastric, pancreatic, and biliary functions by marker-perfusion techniques. Responses to each (S or H) meals differed strikingly both in magnitude and pattern. S meals elicited a stronger early gastric secretory response (acid, pepsin, and volume) which compensated for faster initial emptying and resulted in higher gastric acidity and volume than after H meals. Further, nutrients ingested with S meals were emptied at a slower rate than H (as evidenced by a more gradual decline in intragastric buffer and osmolality, as well as time required for complete emptying of the meal). This, in turn, prolonged pancreatic and biliary responses since stimulation of these organs continued for as long as meal was delivered into the duodenum. However, early biliary outputs (gallbladder response) were less after S than H, probably because nutrients entered the duodenum more slowly and were initially diluted by rapidly emptying water. The physical characteristics of each meal (encompassing appearance, taste, and form of ingestion) probably accounted for early differences in digestive responses. Later, interactions between gastric (motor and secretory), pancreatic, and biliary functions played a major role. Our findings suggest that gastric, pancreatic, and biliary responses to liquid test meals introduced into the stomach may differ substantially from the presumably more physiological response to ordinary solid-liquid meals.

Meals have often been employed in studies of gastrointestinal function in man. Their composition has varied from aqueous solutions of amino acids (1, 2) or peptone (3, 4) to liquid formula meals incorporating carbohydrates, fat, and protein in varying proportions (5, 6) and homogenized natural foods and water (7, 8). Recently, ordinary solid-liquid meals have been utilized for quantification of postprandial gastric function in man (9, 10).

Even if solid and liquid test meals were of similar composition, including volume and caloric value, physical differences might influence digestive functions. Components of liquid meals are more likely to be homogeneously dispersed and therefore discharged together into the duodenum, whereas mixed solid-liquid meals may separate in the stomach into different physical phases, which may empty independently (11-13). In addition, ordinary sol-

Dr. Summerskill died March 9, 1977.

From the Gastroenterology Unit, Mayo Clinic and Mayo Foundation, Rochester, Minnesota 55901.

This investigation was supported in part by Research Grant AM 6908 from National Institutes of Health.

Address for reprint requests: Dr. Juan-R. Malagelada, Gastroenterology Unit, Mayo Clinic, Rochester, Minnesota 55901.

0163-2116/79/0200-0101$03.00/1

id meals more likely trigger cephalic stimulation of gastric (14, 15) and pancreatic (16) functions than liquid meals.

To compare digestive responses to meals of different physical composition, we have fed healthy individuals an ordinary mixed solid-liquid meal or a homogenized meal, each of identical content. Gastric, pancreatic, and biliary functions during digestion were then quantified.

MATERIALS AND METHODS

Volunteers. Six healthy volunteers, four males and two females, mean age 39.7 ± 7.1 (± SE) years, participated in these studies after giving informed consent.

Meal. The meal consisted of 90 g (uncooked weight) tenderloin steak seasoned with 0.1 g salt; 25 g white bread with 8 g butter; and 60 g vanilla ice cream topped with 35 g chocolate syrup. The total caloric value was 458 calories, distributed as approximately 40% carbohydrate, 40% fat, and 20% protein. When the meal was to be eaten, the steak was coarsely ground to facilitate chewing and a glass of water (240 ml) was drunk with the solid meal (S meal). When the meal was to be homogenized, it was blenderized (Waring Blender) with the addition of the same amount of water (H meal) and then delivered intragastrically via a tube. After homogenization, the volume, osmolality, and pH of the meal were 400 ml, 540 mOsm, and 6.0, respectively.

Method for Quantification of Gastric, Pancreatic, and Biliary Functions. The methods for quantification of postprandial volume of gastric contents and its fraction emptied into duodenum; acid, pepsin, and total secretory outputs; and gastric emptying of meal and secretions have been reported by us in detail (9). In brief, following an overnight fast, volunteers swallowed a triple-lumen duodenal tube and a single-lumen gastric tube. One lumen of the duodenal tube was used for continuous perfusion of normal saline (2 ml/min) containing a nonabsorbable marker (PEG 4000, 5 g/liter), being placed adjacent to the papilla of Vater. A second lumen was employed for continuous sampling of duodenal contents 20 cm distally to the perfusion site, at the ligament of Treitz. The third lumen was a duodenal air vent to facilitate suction. A gastric tube, sited in the antrum, was used for repeat sampling of gastric contents after ingestion of meals (either S or H). These contained another nonabsorbable marker ([^{14}C]PEG, 30 μCi, specific activity 0.5 μCi/mg) dissolved in the water. Our previous studies (17) exclude an effect of transpyloric intubation on gastric emptying or secretory responses to a similar meal.

At 10-min intervals after ingesting the meal, gastric and duodenal samples were obtained. [^{14}C]PEG and PEG 4000 concentrations in gastric and duodenal aspirates were measured as previously described (9). The duodenal perfusion system quantified the output of the meal marker into the duodenum, allowing calculation of the amounts remaining in the stomach at each interval after ingestion. Since the concentration of meal marker in the stomach was measured in each gastric sample, the volume of gastric contents and its fraction emptied into the duodenum could be estimated (9). It is important to point out that by determining the [^{14}C]PEG concentration in each gastric sample relative to its total volume (comprising both the aqueous phase and suspended solid particles), we can claim that our measurements of intragastric volume indeed represented the total volume of gastric contents. The only intragastric material excluded in this quantification would have been the very large food particles not retrievable via the tube and the lipid phase, both of which, in terms of *volume*, would account for a minimal fraction of gastric contents. Calculated recovery of the meal marker ([^{14}C]PEG) was 84.6 ± 1.4 (mean ± SE) for the S meal and 91.2 ± 4.8 for the H meal and was not significantly different ($P > 0.05$).

Gastric samples were also analyzed for acid (by titration with 0.05 N NaOH to pH 6.0, identical with that of the meal) and for pepsin activity (18). This allowed calculation of outputs of acid, pepsin, and total secretory volume as previously described (9). Soluble buffer concentrations in gastric samples were measured by comparison with pure gastric juice during titration with 0.1 N NaOH after acidification to pH < 2.0 with 1 N HCl as described by Fordtran and Walsh (10). The term soluble buffer is utilized to represent operational buffer in the liquid phase as opposed to potential buffering power contained in larger solid meal particles in the stomach. The latter, however, would constitute a source of soluble buffer as intragastric digestion progressively disintegrated the swallowed chunks of meat.

Trypsin and bile acid concentrations were determined in duodenal aspirates (pooled at 30-min intervals) as previously described (5) and outputs of these substances quantified by reference to PEG 4000 concentrations (5). The osmolality of gastric duodenal aspirates was measured with a vapor-pressure osmometer (Wescor Inc. Model 5100, Logan, Utah). Blood was obtained immediately before the meal and (beginning 15 min after it was given) at 30-min intervals thereafter until the study was completed. Serum gastrin concentrations were measured by radioimmunoassay (19).

Experimental Design. Each individual was studied on two different days after ingesting the S or H meal, which were given in a randomized sequence. At 7 AM, gastric and duodenal tubes were positioned under fluoroscopic control. Subsequently, basal gastric, pancreatic, and biliary outputs were quantified for 1 hr as described (9). Gastric aspiration was then discontinued, but duodenal perfusion continued and volunteers sat up (until the end of the study). The meal was then presented to the volunteer who was unaware, until then, of which meal (S or H) would be served. On one day (S meal), volunteers were asked to chew the food well, drinking the water (containing [^{14}C]PEG) between bites and swallowing the entire meal over a period of 10 min. On another day (H meal), it was delivered in 10 min into the stomach via the gastric tube. Under both circumstances, gastric and duodenal samples were obtained at 10-min intervals until the stomach was completely empty of food. At this point, gastric contents were entirely aspirated and virtually complete emptying of the stomach was confirmed by lavage with

TABLE 1. STATISTICAL EVALUATION OF FUNCTION CHANGE BY VARIANCE ANALYSIS

Parameter	Factor: Meal (H vs S)* P	Factor: Meal vs time† P
Volume of gastric contents	0.007	<0.001
Rate of gastric emptying	0.025	<0.001
Gastric osmolality	0.56	<0.001
Duodenal osmolality	0.007	<0.001
Gastric pH	0.08	0.001
Titratable acidity	0.01	<0.001
Gastric acid content	0.001	<0.001
Acid output	<0.001	0.049
Pepsin output	<0.001	<0.001
Secretory volume output	<0.001	<0.001
Acid delivery into duodenum	<0.001	0.8
Duodenal pH	0.16	0.21
Gastric buffer content	0.64	<0.001
Trypsin output	0.22	0.13
Bile acid output	0.29	<0.001
Serum gastrin	0.12	0.61

*Demonstrates differences in overall responses to each meal.
†Demonstrates differences between meals in terms of variations of each parameter in relation to time (profile differences).

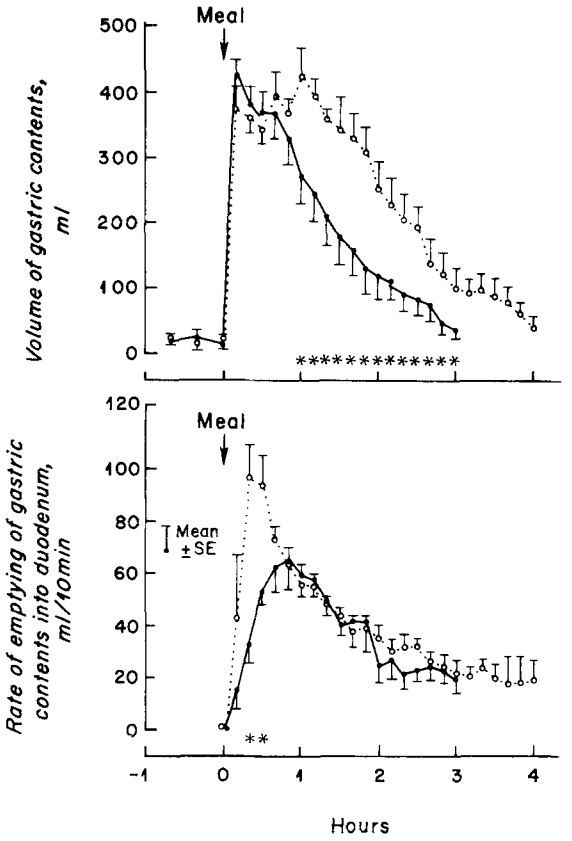

Fig 1. Volume of gastric contents (upper panel) and rate of gastric emptying (lower panel) after meals. (○ represents solid meal; ●, homogenized meal.)

250 ml of normal saline. The H meal was delivered via the gastric tube, as is often performed in studies employing liquid test meals and also to avoid any unpleasant effects which could derive from drinking the blenderized meal.

Statistical Analysis. Results were analyzed as follows: (1) For the 10-min samples after ingestion of the meal, measurements (S vs H) were compared by the paired Student's t test. Significant differences ($P < 0.05$) are indicated in each figure by an asterisk. (2) The full postprandial profile of each parameter studied (ie, acid output, volume emptied, etc) was compared (S vs H) by three-way analysis of variance (20) to determine whether overall responses to meals differed or whether variations of each parameter occurred in relation to time elapsed (Table 1).

RESULTS

Postprandial Volume of Gastric Contents and Gastric Emptying Rate. Marked differences in postprandial volume of gastric contents were found between S and H meals. After ingestion of S meals, intragastric volume remained stable for 1 hr and then decreased progressively as the meal was emptied. In contrast, the volume of gastric contents started to decrease immediately after ingestion of H meals, so that at every interval after 1 hr intragastric volume was significantly lower than after S meals (Figure 1).

Food disappeared significantly faster from the stomach after H than S meals—178 ± 14 min (mean ± SE) vs 220 ± 11 min ($P < 0.01$)—as judged from the time at which no food particles were visible in aspirated gastric contents. The output of gastric contents into the duodenum, representing the rate of gastric emptying, also differed, but only during the first hour (Figure 1) when about twice the volume of gastric contents entered the duodenum after S than H meals.

Intragastric pH, Titratable Acidity, and Gastric Acid Content. Shortly after the meals, intragastric

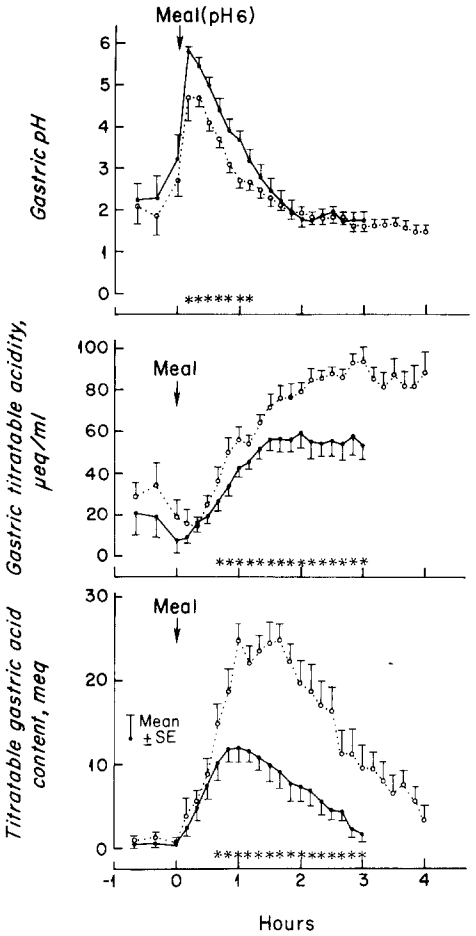

Fig 2. Gastric pH (upper panel), titratable acidity (middle panel), and total acid content (lower panel) after meals. (○ represents solid meal; •, homogenized meal.)

pH started to decline and 2 hr later had reached pH < 2.0 for both meals. The pH was lower after S meals than after H during the first hour. Thereafter, pH remained similar for both until the end of the study (Figure 2). Titratable acid rose faster after S meals and, in contrast to pH, differences between meals progressively enlarged (Figure 2). Total gastric acid content was significantly greater after S meals than H throughout the postprandial period (Figure 2), reflecting the higher titratable acidity and volume of gastric contents.

Acid, Pepsin, and Total Secretory Outputs. S meals elicited much greater acid, pepsin, and total secretory outputs than H meals during the first hour p.c. (Figure 3). Apart from different magnitudes, the secretory profiles of both meals were similar. Acid, pepsin, and total secretory outputs peaked during the first hour after both meals, declining towards the basal level after the second hour.

Soluble Buffer Capacity of Gastric Contents. Gastric soluble buffer concentrations and total soluble buffer content (mainly representing meal protein) peaked shortly after ingestion of H meals and then decreased progressively as the meal was diluted by gastric secretions and emptied (Figure 4). In contrast, after S meals, soluble gastric buffer content increased gradually during the first hour, consistent

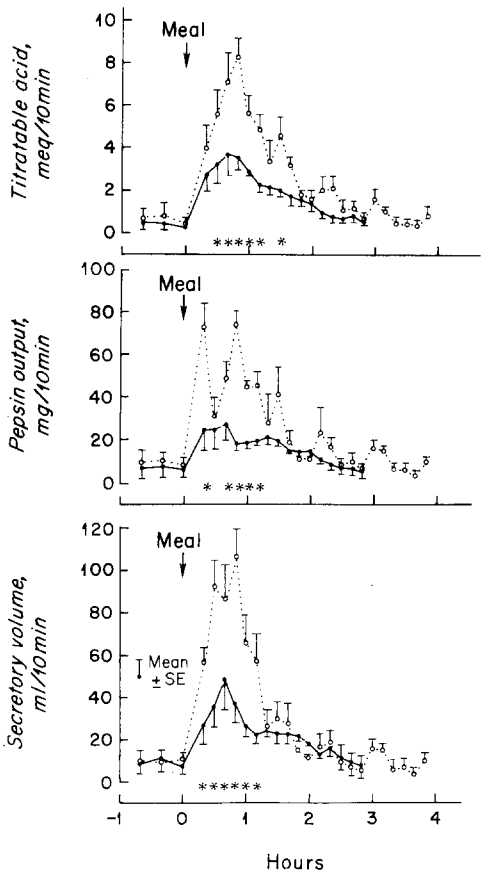

Fig 3. Gastric acid (upper panel), pepsin (middle panel), and secretory volume (lower panel) outputs after meals. (○ represents solid meal; •, homogenized meal.)

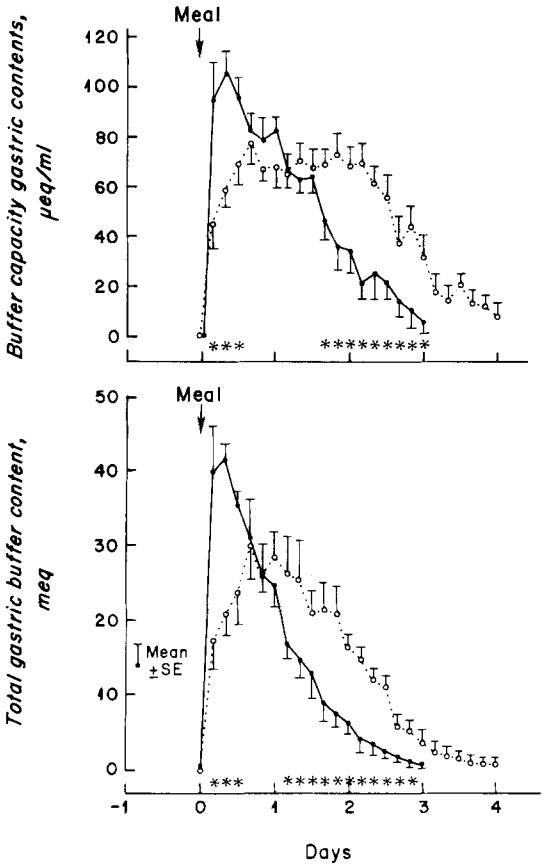

Fig 4. Buffer capacity of gastric contents (upper panel) and total gastric buffer content (lower panel) after meals. (○ represents solid meal; •, homogenized meal.)

with generation of buffer from insoluble larger solid particles of food in the stomach. This never reached the amount of soluble buffer attained after H meals. During the second and third hours, soluble gastric buffer content and concentration after S meals declined, but not as fast as with H (Figure 5), explaining similar intragastric pH during the third hour despite higher titratable acidity produced by S meals.

Osmolality of Gastric and Duodenal Contents. Fasting gastric contents were slightly hyposmolar. Shortly after the H meal, the osmolality of gastric contents resembled that of the meal itself (540 mOsm), whereas, after S, it was much lower (Figure 5), probably on account of the larger size of swallowed solid food fragments and greater dilution by hyposmolar gastric juice. In contrast, during the second and third hours, gastric osmolality decreased faster after H than S meals, presumably because of slower emptying and digestion of solids which generated osmotically active particles.

Distal duodenal osmolality varied, depending on the osmolality of gastric contents emptied into the duodenum. Thus, during the first hour p.c., distal duodenal osmolality was higher after H than S meals, although differences were not as pronounced as in the stomach (Figure 5). Beyond the first hour, distal duodenal osmolality was maintained nearly isotonic for both meals despite marked differences in gastric osmolality.

Titratable Acid Emptied into Duodenum and Distal Duodenal pH. After both meals, acid was delivered into the duodenum at relatively uniform rates

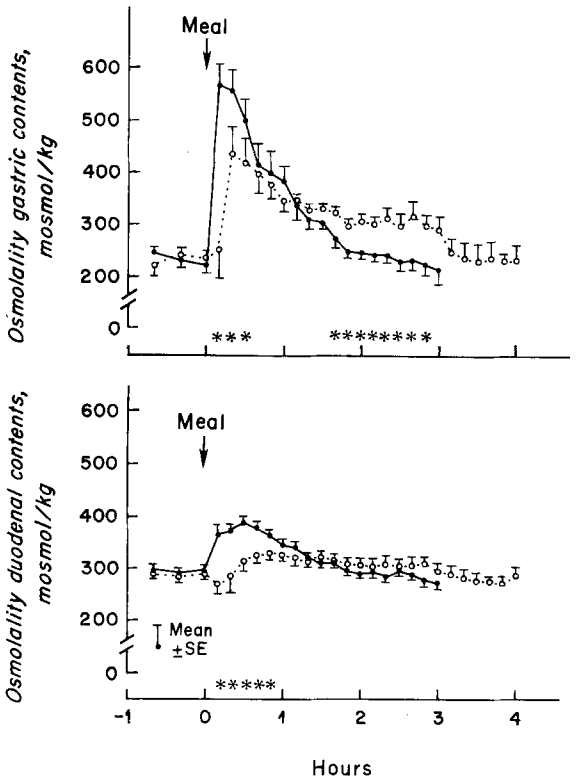

Fig 5. Gastric (upper panel) and duodenal (lower panel) osmolality after meals. (○ represents solid meal; •, homogenized meal.)

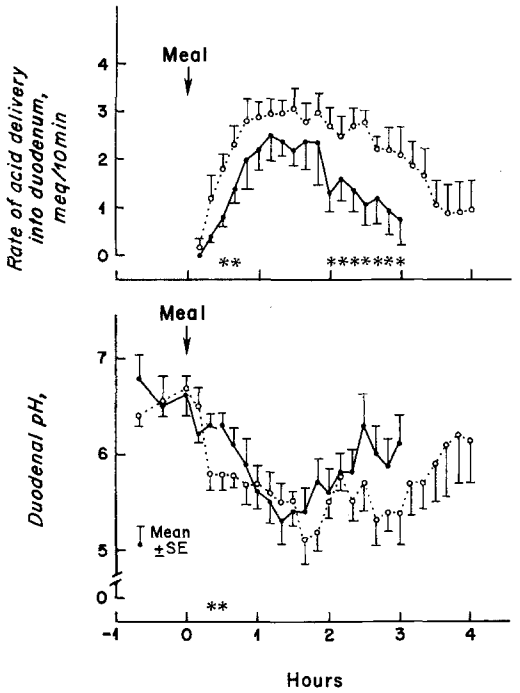

Fig 6. Rate of acid entering duodenum (upper panel) and duodenal pH (lower panel) after meals. (○ represents solid meal; ●, homogenized meal.)

despite fluctuating gastric acid outputs (Figure 6 vs Figure 3). Although overall acid output into the duodenum was greater after S meals, peak rates of acid delivery were similar (Figure 6). Thus, the greater amounts of acid secreted by the stomach in response to S meals reached the duodenum over a longer period of time, but not much faster, than after H meals.

Acid entering the duodenum after meals produced a corresponding decrease in the pH of duodenal contents (Figure 6), as measured in the distal duodenum. The lowest intraduodenal pH recorded (between 1 and 2 hr) was similar for both H and S meals (5.3 ± 0.2, mean ± SE, and 5.1 ± 0.3 pH units, respectively). Intraduodenal pH then gradually rose towards baseline as both meals were emptied from the stomach.

Pancreatic Enzyme and Biliary Outputs. Trypsin output increased rapidly after both S and H meals, peaking within the first hour. The outputs then gradually declined towards basal values, but this decrease occurred earlier and was more pronounced after H meals (Figure 7), which were emptied faster from the stomach.

Bile acid output during the first hour (reflecting greater gallbladder contraction) was, in contrast, greater after H meals but later declined towards basal faster than after S meals, thus paralleling pancreatic enzyme output (Figure 7). Cumulative bile acid output after S meals (6.57 ± 0.68 mmol, mean ± SE) was not significantly different ($P > 0.05$) from that after H meals (5.59 ± 0.48 mmol).

Serum Gastrin Concentrations. Serum gastrin responses were similar after both meals. Gastrin lev-

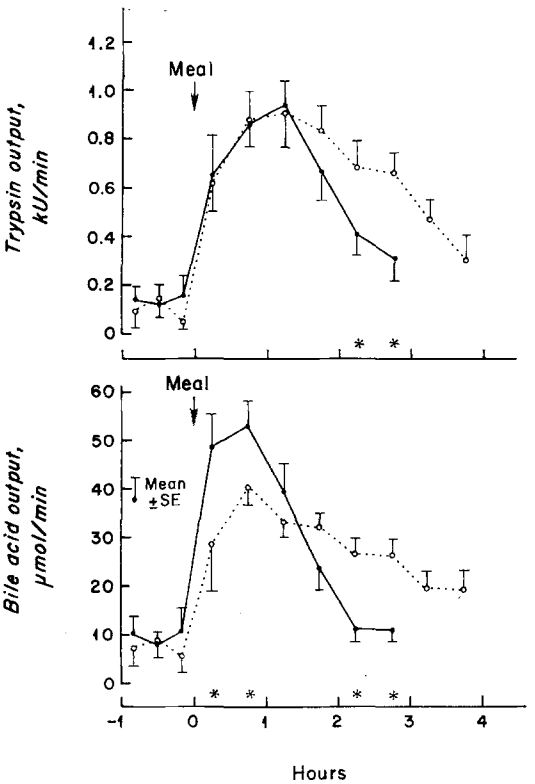

Fig 7. Pancreatic enzyme (upper panel) and bile acid (lower panel) outputs after meals. (○ represents solid meal; ●, homogenized meal.)

els peaked within the first hour after ingestion of food in most individuals. Thereafter, serum gastrin concentrations continuously decreased towards basal values following an identical pattern after both meals (Figure 8).

Analysis of Variance of Postprandial Measurements. Analysis of variance was performed to compare the complete postprandial response to S and H meals for each individual parameter (Table 1). By this method, the postprandial volume of gastric contents and their rate of emptying into the duodenum; duodenal osmolality; gastric titratable acidity and gastric acid content; acid, pepsin, and total secretory outputs were overall higher after S than H meals. Also, significant differences were found in the way these parameters varied in relation to time elapsed from ingestion of each meal (profile differences).

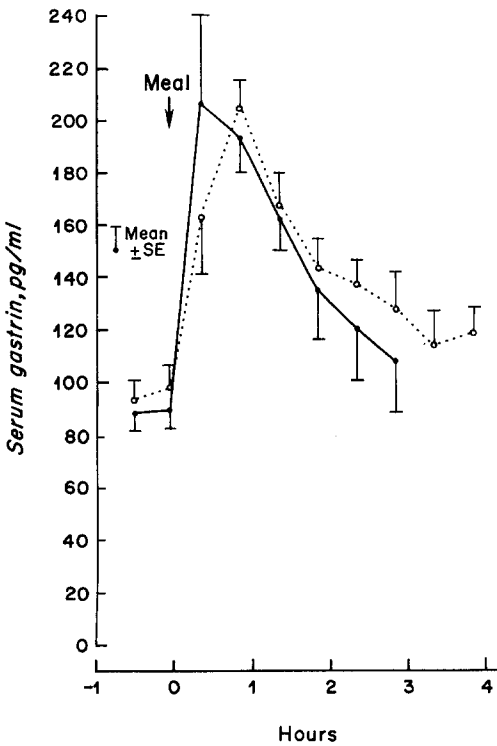

Fig 8. Serum gastrin response to meals. (○ represents solid meal; ●, homogenized meal.)

We found significant profile differences (but not in overall responses) between meals in postprandial gastric osmolality, pH and buffer content, and bile acid outputs (Table 1). In contrast, acid emptying into the duodenum was, overall, significantly greater after S than H meals but profiles were similar (Figure 6). Duodenal pH and trypsin outputs after S and H did not differ significantly by analysis of variance although occasional significant differences were noted at some intervals during the study (Figures 6 and 7, respectively).

DISCUSSION

Our study demonstrates that conventional solid-liquid meals (S) eaten in the usual manner evoke different gastric, pancreatic, and biliary responses than identical meals delivered intragastrically in homogenized form (H). Several factors may be responsible for higher acid, pepsin, and volume outputs evoked by S meals during the first hour (when gastric secretory activity normally peaks) (9): First, greater stimulation of the cephalic phase of gastric secretion presumably occurred with S meals, which were more appealing, and, unlike H meals, were tasted and chewed (15). However, since volunteers were unaware of which meal they would receive until it was served, psychic anticipatory effects (14) were at least diminished. Second, a large fraction of ingested water was quickly emptied into the duodenum after S meals (see later), perhaps increasing the local stimulatory effects of remaining nutrients on gastric secretion (21). Third, in part as a result of higher gastric secretory rates, the volume of gastric contents after S meals exceeded that after H meals, thus perpetuating the secretory stimulus through antral distension (22). Finally, the mechanical stimulus exerted by solid particles may have enhanced secretory outputs after S meals (as opposed to finely dispersed particles in H meals). Similar serum immunoreactive gastrin concentrations after both meals suggest that different gastric secretory outputs were not due to differences in gastrin release.

Some methodological considerations are pertinent when comparing gastric responses to S or H meals suggest that different gastric secretory outputs were not due to differences in gastrin release. present in the stomach only after S meals. These particles elude quantification by our marker dilution system. However, the error they introduce in our measurements of intragastric volume is relatively small in comparison to the much larger mass of fluid

and suspended solids. Secondly, steady-state conditions of the duodenal marker dilution system could be theoretically disturbed to a greater extent by the S meal, which causes rapid emptying of fluids, than by the H meal, which has a more gradual emptying pattern. In practice, however, the accuracy of the method must be similar after both meals since total PEG recovery was the same. Further, our method has been validated (9, 11) for the S meal, which should cause the greatest disequilibrium in the system. It is quite possible that the capability of our technique to accurately quantify rapid variations in duodenal flow might be due to our duodenal aspiration procedure, which, as opposed to fixed-volume sampling, should accommodate better to the ideal conditions of recovery proportional to intraluminal flow postulated by Levitt and Bond (23). Thirdly, a discrepancy might exist between S and H meals in the size and number of solid particles which might buffer acid and bind pepsin yet leave the stomach at different rates than liquids (11). However, the same differences observed in acid and pepsin outputs between S and H meals were observed in total secretory volume output, suggesting that binding to retained solid particles is unlikely to account for the different response to the meals. Furthermore, the larger solid particles which would be retained longer should have a much smaller binding surface area, relative to their weight, than the finely dispersed particles which leave the stomach with fluids.

Interplay between gastric secretion and emptying had reciprocal effects on these functions and ultimately determined pancreatic and biliary responses to each meal. Thus, S meals elicited a strong early gastric secretory response which balanced the more rapid initial emptying and resulted in a larger and steadier intragastric volume than after H meals. Responses to the latter, in contrast, were characterized by a lower secretory response which was insufficient to compensate for gastric emptying. The result was a smaller volume of gastric contents after H meals which progressively declined from the time of ingestion. The well-known differential emptying of liquids and solids after a mixed meal (11, 13), as opposed to more uniform emptying of the liquid meal, was probably responsible for the observed differences in gastric emptying after each meal. Plain water ingested with S meals leaves the stomach rapidly (11) whereas the higher osmolality of the homogenized meal would have resulted in slower initial emptying (24). As digestion of meals proceeded, gastric soluble buffer content and gastric osmolality after S meals gradually became greater than after H. This reflected both slower gastric emptying of ingested solid food and generation of new buffer and osmotically active particles from disintegration and digestion of meat. Slower emptying of solids and an expanded volume of gastric contents (because of larger gastric secretory volume) delayed by one hour the time needed to completely empty the nutrients in the S meal as compared to H. Thus, our observations support the empirical clinical concept that liquid diets reduce gastric secretory responses and accelerate evacuation of nutrients. Formula test meals, studied by us (5) and others (6), exhibit an overall emptying pattern which resembles that of our H meal, although differences in caloric value and composition of meals preclude strict comparison of results. There are no relevant data concerning S-type meals.

Rates of delivery of acid into the duodenum after S meals were consistently greater than after H meals, although *peak* delivery rates (between 1-3 hr) did not differ significantly and both meals produced similar falls in distal duodenal pH during that period. Thus, delivery into the duodenum of the larger amounts of acid evoked by S meals was accomplished through a longer duration rather than by higher peak delivery rates. This is consistent with the participation of acid-sensitive mechanisms in the duodenum (25) which assist uniform delivery of acid.

Although pancreatic enzyme output was identical for both meals during the first and second hours, it gradually returned to baseline after H meals (which were rapidly emptied from the stomach) during the third hour, whereas secretion continued after the more slowly emptied S meals. The peak postprandial trypsin outputs measured after both meals resembled those earlier reported by us in response to high doses of intravenous cholecystokinin (CCK): 0.25 Crick-Harper-Raper units/kg/min (26). Similar pancreatic enzyme responses have been achieved by intraduodenal perfusion with high concentrations of fatty acids (27) or calcium (28) as well as Lundh-type liquid formula meals (5). Since pancreatic secretion after meals is probably determined by interaction among multiple neurohormonal factors, these observations provide little information as to the actual mechanisms involved. However, they suggest that similar pancreatic enzyme outputs may be achieved by a variety of stimuli, including composite meals.

In contrast, bile acid output in the first hour was smaller after S than H meals, and this may be due to the lesser sensitivity of the gallbladder to both porcine (26) and endogenous (28) CCK, when compared to the pancreas. During the later postprandial period, bile acid outputs (like pancreatic enzyme outputs) declined faster after H meals, presumably because these emptied more rapidly and left the duodenum earlier. Cumulative bile acid outputs were therefore similar for each meal and approximated the size of the normal bile acid pool (29). This agrees with our previous estimation of four enterohepatic cycles during 24 hr in healthy individuals eating three liquid meals of caloric value similar to our current meal (5).

Our study demonstrates that conventional solid-liquid meals eaten in the usual manner elicit different gastric, pancreatic, and biliary responses than identical meals delivered intragastrically in homogenized form. The results point out difficulties in comparing digestive responses to different types of meals as studied in different laboratories. Further, our findings emphasize the physiological importance of a natural physical state and route of ingestion of foods in man.

ACKNOWLEDGMENTS

The authors are indebted to Dr. William F. Taylor for his assistance in statistical analysis; to Mrs. Judith A. Duenes, Ms Ruth Bolton, Ms Cathy DeVos, Mrs. Jane Bailey, and Mr. Richard Tucker for technical assistance; and to Ms Gaurdis Grube for secretarial help.

REFERENCES

1. Walsh JC, Richardson CT, Fordtran JS: pH dependence of acid secretion and gastrin release in normal and ulcer subjects. J Clin Invest 55:462-468, 1975
2. Cooke AR, Moulang J: Control of gastric emptying by amino acids. Gastroenterology 62:528-532, 1972
3. Konturek SJ, Biernat J, Oleksy J: Serum gastrin and gastric acid responses to meals at various pH levels in man. Gut 15:526-530, 1974
4. Henn RM, Isenberg JI, Maxwell V, Sturdevant RAL: Inhibition of gastric acid secretion by cimetidine in patients with duodenal ulcer. N Engl J Med 293:371-375, 1975
5. Brunner H, Northfield TC, Hofmann AF, Go VLW, Summerskill WHJ: Gastric emptying and secretion of bile acids, cholesterol, and pancreatic enzymes during digestion: Duodenal perfusion studies in healthy subjects. Mayo Clin Proc 49:851-860, 1974
6. Johansson C, Lagerlof JO, Ekelun K, Kulsdom N, Larsson I, Nylind B: Determination of gastric secretion and evacuation, biliary and pancreatic secretion, intestinal absorption, intestinal transit time and flow of water in man. Scand J Gastroenterol 7:489-499, 1972
7. Richardson CT, Bailey BA, Walsh JH, Fordtran JS: The effect of an H_2-receptor antagonist on food-stimulated acid secretion, serum gastrin, and gastric emptying in patients with duodenal ulcers: Comparison with an anticholinergic drug. J Clin Invest 55:536-542, 1975
8. Rhodes J, Barnardo DE, Phillips SF, Rovelstad RA, Hofmann AF: Increased reflux of bile into the stomach of patients with gastric ulcer. Gastroenterology 57:241-252, 1969
9. Malagelada J-R, Longstreth GF, Summerskill WHJ, Go VLW: Measurement of gastric functions during digestion of ordinary solid meals in man. Gastroenterology 70:203-210, 1976
10. Fordtran JS, Walsh JH: Gastric acid secretion rate and buffer content of the stomach after eating. J Clin Invest 52:645-657, 1973
11. Malagelada J-R: Quantification of gastric solid-liquid discrimination during digestion of ordinary meals. Gastroenterology 72:1264-1267, 1977
12. Chang CA, McKenna RD, Beck IT: Gastric emptying rate of the water and fat phases of a mixed test meal in man. Gut 9:420-424, 1968
13. Meyer JH, MacGregor IL, Gueller T, Martin P, Cavalieri R: ^{99m}Tc-tagged chicken liver as a marker of solid food in the human stomach. Am J Dig Dis 21:296-304, 1976
14. Moore JG, Schenkenberg T: Psychic control of gastric acid: Response to anticipated feeding and biofeedback training in man. Gastroenterology 66:954-959, 1974
15. Crawshaw HM, Fraser DM, Warrender TS: Can psychic stimulation cause gastric acid secretion in man? Lancet 2:66-68, 1968
16. Sarles H, Dani T, Prezelin G, Souville C, Figarella C: Cephalic phase of pancreatic secretion in man. Gut 9:214-221, 1968
17. Longstreth GF, Malagelada J-R, Go VLW: The gastric response to a transpyloric duodenal tube. Gut 16:777-780, 1975
18. Berstad A: A modified hemoglobin substrate method for the estimation of pepsin in gastric juice. Scand J Gastroenterol 5:343-348, 1970
19. Sizemore GW, Go VLW, Kaplan EL, Sanzenbacher LS, Holtermuller KH, Arnaud CD: Relations of calcitonin and gastrin in the Zollinger-Ellison syndrome and medullary carcinoma of the thyroid. N Engl J Med 288:641-644, 1973
20. Dixon WJ, Massey FJ, Jr: Introduction to statistical analysis, third edition. New York, McGraw-Hill, 1969
21. Debas HT, Grossman MI: Chemicals bathing the oxyntic gland area stimulate acid secretion in dog. Gastroenterology 69:654-659, 1975
22. Grossman MI: The chemicals that activate the "on" switches of the oxyntic cell. Mayo Clin Proc 50:515-518, 1975
23. Levitt MD, Bond J: Use of the constant perfusion technique in the non-steady state. Gastroenterology 73:1450-1452, 1977
24. Meeroff JC, Go VLW, Phillips SF: Control of gastric emptying by osmolality of duodenal contents in man. Gastroenterology 68:1144-1151, 1975

25. Cooke AR: Duodenal acidification: Role of first part of duodenum in gastric emptying and secretion in dogs. Gastroenterology 67:85-92, 1974
26. Malagelada J-R, Go VLW, Summerskill WHJ: Differing sensitivities of gallbladder and pancreas to cholecystokinin-pancreozymin (CCK-PZ) in man. Gastroenterology 64:950-954, 1973
27. Malagelada J-R, Go VLW, DiMagno EP, Summerskill WHJ: Interactions between intraluminal bile acids and digestive products on pancreatic and gallbladder function. J Clin Invest 52:2160-2165, 1973
28. Holtermuller KH, Malagelada J-R, McCall JT, Go VLW: Pancreatic, gallbladder and gastric functions during intraduodenal calcium perfusion in man. Gastroenterology 70:693-696, 1976
29. Vlahcevic ZR, Bell CC Jr, Swell L: Significance of the liver in the production of lithogenic bile in man. Gastroenterology 59:62-69, 1970