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Contribution of Luminal Concentration of Nutrients and Osmolality to Postprandial Intestinal Hyperemia in Dogs[1] (39462)

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While anticipation and ingestion of food elicit a generalized cardiovascular response by activating the sympathetic nervous system, the cardiovascular adjustments during the postprandial period are limited to a hyperemia in the digestive organs (1-3). The hyperemia begins within 5 to 15 minutes following oral ingestion of food. Recent studies further indicate that the hyperemia in the gastrointestinal tract is confined to the mucosal layer of the segment containing chyme (4-6). These studies suggest that the hyperemia may be related to absorptive processes and/or interaction of chyme with the mucosa. The present study was designed to assess if the concentration of nutrients and/or osmolality of chyme in the gut lumen are significant factors determining the degree of postprandial intestinal hyperemia.

Methods. Fasted mongrel dogs were anesthetized with pentobarbital sodium (30 mg/kg), ventilated with a Harvard respirator, and given heparin sodium (6 mg/kg) as an anticoagulant. A loop of jejunum was exteriorized and divided into two segments, each drained by a single vein (4). The veins were cannulated and the venous outflows were directed into a reservoir from which the blood was pumped back to the animal via a femoral vein. A rubber tube was placed into the lumen of each segment for the introduction and withdrawal of fluids. At all other times, the tube was connected to a Statham pressure transducer (Model No. P23Gb) to monitor intraluminal pressure. Both ends of each segment were tied and the mesentery was cut to exclude collateral flow. Systemic arterial pressure was continuously monitored through a femoral arterial cannula.

Commercially available dog food (Alpo, Allen Products Co., Allentown, Pa.; fat, 7.0%; protein, 12.0%; fiber, 1.5%; moisture, 78.0%; ash, 3.0%) was homogenized and its pH was adjusted to approximately 7.0 with $NaHCO_3$. To each can of this homogenate was added 750 mg of a pancreatic enzyme preparation[2] (Viokase, Viobin Corp., Monticello, Ill.) and the whole mixture was gently stirred with a magnetic stirrer for 5 hr to permit digestion. From this digested food, four mixtures of different concentrations were prepared. One was undiluted (100%); a second was diluted with distilled water to give a mixture which was 33% food in water, i.e., 1 part food, 2 parts water. The third was diluted to give a 20% and the fourth was 10% food in water. Aliquots of each of the four food mixtures were centrifuged (19,250*g*) and the pH and osmolalities of their supernatants determined (Beckman Expandomatic pH meter, Beckman Instruments, Incorporated, Advanced Osmometer, Advanced Instruments, Incorporated). The pH of 100, 33, 20, and 10% food mixtures were 6.40 ± 0.02, 6.53 ± 0.02, 6.57 ± 0.02, and 6.58 ± 0.04, respectively, and the osmolalities were 998.6 ± 30.3, 291.3 ± 5.3, 183.0 ± 5.8, and 94.0 ± 2.7 mOsm/kg (mean ± SEM). Seven and 12 cans of the dog food were treated as described above for the determination of pH and osmolality, respectively.

The protocol for all experiments consisted of three 15-min periods: Precontrol, test, and postcontrol. In the pre- and postcontrol periods, both segments contained 10 ml of normal saline. The luminal contents in the test period varied with each experiment. During the test period of the first series of experiments (N = 7), one segment contained 10 ml of one of the four food mix-

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[2] The pancreatic enzyme preparation did not alter jejunal blood flow when placed into the lumen (unpublished observation).

tures and the other segment 10 ml of normal saline so that the effects of each of these mixtures could be studied using saline as a control in the other segment. In the second series of experiments ($N = 6$), the hyperemic effects of 100, 33, and 20% food mixtures were compared. During the test period, one segment contained 10 ml of one of these three mixtures and the other segment 10 ml of one of the other two mixtures. Since 100, 20, and 10% food mixtures were not isotonic to plasma, the effects of these mixtures might be due, in part, to their osmolalities. The third series of experiments ($N = 6$) was designed to test this possibility. In order to eliminate the hypotonic effect of 20 and 10% food mixtures, isotonic mixtures of these foods (320.0 ± 12.3 and 281.3 ± 6.0 mOsm/kg, respectively) were made from a portion of these mixtures by addition of appropriate amounts of NaCl. During the test period, one segment contained 10 ml of a hypotonic mixture while the other segment contained 10 ml of the isotonic mixture of the same concentration. The hypertonic 100% food could not be made isotonic without decreasing its concentration. Therefore, a 30% solution of a nonabsorbable substance, polyethylene glycol (PEG), having the same osmolality (1000 mOsm/kg) as that of 100% food was made. During a test period, one segment contained 10 ml of 100% food while the other segment contained 10 ml of 30% PEG. In the three series, all solutions introduced into the intestinal lumen were at 37°.

Control or test mixtures remained in the lumen for 15 min during which venous outflows from both segments were simultaneously collected in graduated cylinders in 3-min samples with a 1-min interval between collections. Aliquots of venous blood of the last collection were retained for determination of osmolality (Advanced Instruments Osmometer). After each period, the lumen contents were withdrawn, their volumes measured, and the lumen was gently washed with warm normal saline.

Results. Systemic arterial pressure which ranged from 116 to 165 mm Hg (136.8 ± 2.7 mm Hg, mean ± SEM) in all three series of experiments was not significantly altered by luminal placement of any food mixture, saline, or PEG. After luminal placement of 100, 33, or 20% food mixture, venous outflow gradually increased, reached a plateau by 8 to 11 min, and remained at that level for the next 4 min. The venous outflow measured 8 to 11 min following the placement of any food mixture was statistically the same as that measured during the last 3-min period. Therefore, only the values from the last 3-min flow collection were used for expressing and analyzing the data.

Series I (Table I). Luminal placement of 100, 33, or 20% digested food mixture significantly increased venous outflow, but 10% food did not. No significant change in flow occurred in the control segment into which normal saline was placed successively in the three periods. The lumen volume significantly increased (+2.5 ± 0.8 ml) with 100% food in the lumen, did not change with saline, 33 or 20% food, and decreased with 10% food (−3.5 ± 0.8 ml). Only 100% food significantly increased venous osmolality (+10.6 ± 2.4 mOsm/kg from a control of 293.3 ± 1.6 mOsm/kg).

Series II (Table II). The hyperemic effect of luminal placement of 100% food was significantly greater than that of 33 or 20% food (comparisons 1 and 2). The hyperemic effect of 33 and 20% food mixtures was similar. Again, only 100% food in the lumen significantly increased lumen volume and venous osmolality.

Series III (Table III). While 100% food markedly increased flow, 30% PEG did not significantly alter flow. Both solutions, however, equally increased venous osmolality and lumen volume. Both isotonic and hypotonic 20% food mixtures increased flow to the same extent and did not significantly alter venous osmolality or lumen volume. Neither isotonic nor hypotonic 10% food significantly altered flow, but hypotonic 10% food significantly decreased lumen volume.

Discussion. The aim of this study was to assess if the concentration of nutrients and the osmolality of chyme in the intestinal lumen are significant factors determining the degree of intestinal hyperemia during

TABLE I. MEAN ± SEM VENOUS OUTFLOW (ML/MIN/100G) FROM TWO ADJACENT JEJUNAL SEGMENTS[a].

	Experimental segment			Control segment		
Lumen content	Saline	Food	Saline	Saline	Saline	Saline
100% food	47.4 ± 5.7	65.6 ± 6.6[b]	47.7 ± 6.6[b]	55.1 ± 8.4	51.8 ± 8.5	59.1 ± 11.7
33% food	57.0 ± 9.8	66.5 ± 10.4[b]	52.9 ± 8.1[b]	51.7 ± 7.7	47.1 ± 6.7	46.3 ± 5.8
20% food	49.4 ± 7.9	60.5 ± 8.3[b]	50.5 ± 6.6[b]	51.4 ± 6.9	50.8 ± 5.8	46.1 ± 5.7
10% food	55.3 ± 7.6	59.0 ± 8.6	54.4 ± 9.5	59.2 ± 12.4	54.3 ± 11.7	52.6 ± 11.8

[a] $N = 7$ for each food mixture.
[b] Value significantly different from preceeding value, $p < 0.05$ (paired Student's t test).

TABLE II. COMPARISON OF THE EFFECTS OF LUMINAL PLACEMENT OF 100, 33, AND 20% FOOD ON VENOUS OUTFLOW, VENOUS OSMOLALITY, AND LUMEN VOLUME[a]

	Segment A	Segment B	D = A − B[b]
Comparison 1	100% food	33% food	
Blood Flow (%)	+26.9 ± 4.4[c]	+10.4 ± 1.3[c]	+16.5 ± 5.9[c]
Osmolality (mOsm/kg)	+8.3 ± 2.3[c]	+1.5 ± 1.3	+6.8 ± 2.1[c]
Lumen volume (ml)	+1.9 ± 0.1[c]	+0.2 ± 0.4	+1.7 ± 0.4[c]
Comparison 2	100% food	20% food	
Blood flow (%)	+24.4 ± 6.2[c]	+10.3 ± 2.9[c]	+14.1 ± 4.5[c]
Osmolality (mOsm/kg)	+10.5 ± 2.5[c]	+0.8 ± 1.2	+9.7 ± 3.4[c]
Lumen volume (ml)	+2.1 ± 0.7[c]	−0.5 ± 0.4	+2.6 ± 0.9[c]
Comparison 3	33% food	20% food	
Blood flow (%)	+18.3 ± 4.0[c]	+17.3 ± 4.7[c]	+1.0 ± 2.4
Osmolality (mOsm/kg)	+2.0 ± 1.3	+0.0 ± 0.6	+2.0 ± 1.2
Lumen volume (ml)	+0.4 ± 0.3	−0.6 ± 0.7	+1.0 ± 0.5

[a] N = 6 for each comparison. The values are changes from precontrol values. Comparisons 1 and 2 were performed in the same animals with food from the same cans, but comparison 3 was performed in another group of animals. Data from the latter group are also presented in Table III.
[b] D = the difference in changes produced by two paired food mixtures.
[c] Values are statistically significant, $p < 0.05$ (paired Student's t test).

digestion. As shown in Table I, luminal placement of 100, 33, or 20% food mixture significantly increased venous outflow, in contrast, placement of a 10% food mixture did not significantly alter flow. These data suggest that the concentration of nutrients in the lumen must exceed a certain value to produce local hyperemia. The hyperemic effect of 100% food was significantly greater than that of 33 or 20% food (comparisons 1 and 2, Table II) indicating that the greater the concentration of nutrients in the chyme the greater is the resultant hyperemia. However, a slight difference in the concentration does not appear to produce an appreciable difference in the hyperemic effect because 33 and 22% food mixtures increased flow to the same extent (comparison 3, Table II).

Since the osmolalities of the four food mixtures are different, the differences in their vascular effects may be due to the differences in their osmolalities. However, as shown in Table III, a 30% PEG solution having the same osmolality as 100% food does not significantly alter venous outflow even though its effects on venous osmolality and lumen volume are qualitatively and quantitatively similar to those of 100% food. The hyperemic effect of 100% food therefore is not due to its hypertonicity. Also, neither the hyperemic effect of 20% food nor the lack of vascular effect of 10% food is due to their hypotonicity. As shown in Table III, keeping the concentrations of nutrients in the mixtures unchanged but raising their osmolalities to near isotonicity does not alter the vascular effects of the hypotonic 20 or 10% food mixtures. These data thus indicate that lumen osmolality, within a range of 180 to 1000 mOsm/kg is not a significant factor contributing to the local intestinal hyperemia produced by the presence of chyme in the jejunal lumen. We have also shown previously that changes in

TABLE III. COMPARISON OF THE EFFECTS OF LUMINAL PLACEMENT OF HYPERTONIC PEG AND 100% FOOD, ISO- AND HYPOTONIC 20% FOOD, AND ISO- AND HYPOTONIC 10% FOOD ON THE VENOUS OUTFLOW, VENOUS OSMOLALITY, AND LUMEN VOLUME[a].

	Segment A	Segment B	D = A − B[b]
Comparison 1	100% food	30% PEG	
Blood flow (%)	+37.4 ± 7.9[c]	+1.4 ± 2.2	+36.0 ± 6.5[c]
Osmolality (mOsm/kg)	+13.2 ± 3.9[c]	+13.7 ± 5.0[c]	−0.5 ± 5.1
Lumen volume (ml)	+3.3 ± 0.7[c]	+4.2 ± 0.6[c]	−0.9 ± 0.7
Comparison 2	I-20% food	H-20% food	
Blood flow (%)	+18.7 ± 6.6[c]	+18.9 ± 6.8[c]	−0.2 ± 3.5
Osmolality (mOsm/kg)	+4.3 ± 1.9	+0.5 ± 2.0	+3.8 ± 3.7
Lumen volume (ml)	−0.4 ± 0.5	−0.9 ± 0.8	+0.5 ± 0.7
Comparison 3	I-10% food	H-10% food	
Blood flow (%)	+3.1 ± 7.9	+7.6 ± 5.4	−4.5 ± 5.0
Osmolality (mOsm/kg)	+2.3 ± 2.9	−5.3 ± 2.9	+7.6 ± 4.9
Lumen volume (ml)	−1.3 ± 7.4	−4.3 ± 1.0[c]	+3.0 ± 0.7[c]

[a] $N = 6$ for each comparison. The values are changes from precontrol values. I-20% and I-10% = Isotonic 20% and 10%. H-20% and H-10% = Hypotonic 20% and 10%.

[b] D = the difference in changes produced by two paired food mixtures.

[c] Values are statistically significant, $p < 0.05$ (paired Student's t test).

lumen pH, over a range of 2.5 to 11.0, do not significantly alter local blood flow (7, 8).

The finding that the hyperemia requires a presence of a certain amount of digested food in the lumen and is directly related to the concentration of digested food in the chyme suggests that some chemicals in the food mixture are vasoactive when placed into the lumen. We have found recently that the pancreatic enzyme preparation used in this present study is not vasoactive when placed into the lumen. We have also found that the vasoactive substances are suspended in the supernatant of the digested food since luminal placement of the supernatant increases blood flow, but placement of the precipitate or undigested food do not (unpublished observation). The vasoactive chemicals therefore seem to be digestive products of carbohydrates, lipids, and/or proteins. We have shown that glucose increases intestinal blood flow when placed into the lumen and the greater the concentration the greater is the hyperemia (4).

Summary. Intestinal blood flow is increased during digestion. This study assesses if the concentration of nutrients and/or osmolality of chyme in the intestinal lumen are factors determining the hyperemia. Six digested food mixtures containing different concentrations of nutrients and/or having different osmolalities were placed into the jejunal lumen, and their effects on local venous outflow compared. The 100% (999 mOsm/kg), 33% (291 mOsm/kg), and 20% (183 mOsm/kg) food mixtures all increased flow, but the 10% food mixture (94 mOsm/kg) did not. The hyperemic effect of 33 and 20% food was similar, but 100% food produced a greater increase in flow than did 33 or 20% food. Luminal placement of a 30% solution of a nonabsorbable substance polyethylene glycol (1000 mOsm/kg) did not alter flow. Also, the vascular effects of 20 or 10% food mixtures were not altered when these mixtures were made isotonic by the addition of NaCl. These studies indicate that lumen osmolality, within a range of 180 to 1000 mOsm/kg, is not a significant factor contributing to the local hyperemia occurring when nutrients are in the gut lumen. However, the concentration of nutrients in the lumen is a factor determining the local hyperemia.

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