Response of the Canine Duodenum to Intraluminal Challenge with Cholera Exotoxin

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ABSTRACT In response to intraluminal challenge with crude cholera exotoxin, canine Thiry-Vella duodenal loops consistently produced isotonic fluid for a 24–36 hr period. Isotonic fluid production generally began within 15 min after challenge. Mean bicarbonate concentration of fluid produced by duodenal loops was 24 ±6 (SD) mEq/liter. Perfusion of exotoxin-treated duodenal loops with an isotonic electrolyte solution containing glucose 60 mOsm/liter caused a significant decrease in exotoxin-induced isotonic fluid output. The net effects of glucose on isotonic fluid absorption by perfused duodenal loops were not significantly different before and after administration of crude cholera exotoxin.

The response of canine duodenal loops to challenge by cholera exotoxin differs from responses of jejunal and ileal loops in *a*) absence of a detectable "lag period" between administration of exotoxin and initiation of net fluid output; *b*) a longer period of fluid production following exotoxin administration; and *c*) a significantly greater net fluid output per unit length of gut. The mean bicarbonate concentration of the fluid produced by duodenum is less than that produced by ileum, but is not significantly different from that produced by jejunum. The duodenal response is similar to that of the more distal small bowel segments in that an effect on isotonic fluid movement is observed shortly after exotoxin administration and the maximum rate of exotoxin-induced isotonic fluid production is not reached until 4–5 hr after exotoxin administration. The basis for the consistent delay of 4–5 hr between intraluminal exotoxin administration and maximum gut fluid production has not yet been determined.

Current data are consistent with the hypothesis that the rate of secretion of isotonic fluid induced by cholera exotoxin is not significantly different per unit length, in duodenum and ileum and that the lesser *net* fluid output in the ileum is due to the greater capacity for isotonic fluid absorption by the more distal small bowel segment.

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INTRODUCTION

Recent studies have demonstrated that the electrolyte loss in experimental canine cholera originates in the small bowel. Although the major portion of the electrolyte is secreted by jejunum and ileum, electrolyte loss has also consistently been observed proximal to the ligament of Treitz (1). When crude cholera exotoxin has been administered intraluminally to chronic canine Thiry-Vella fistulae of jejunum or ileum, a significant "lag period" has consistently been observed between the time of intraluminal administration of exotoxin and net fluid output by the small bowel loops (2). After the "lag period" there is a steady increase in fluid output until the 4th or 5th hr after exotoxin challenge. The "lag period" is greater in ileum than jejunum, but the maximal rate of fluid production is reached at approximately the same time in both segments of small bowel (2). The cholera exotoxin appears to act by inducing hypersecretion of electrolyte into the bowel lumen, and does not significantly alter absorption of sodium from bowel lumen in man (3) or the experimental animal (4, 5). It has been postulated that the cholera exotoxin may have an appreciable ef-

fect on small bowel secretion shortly after its administration, but that this early effect is masked by continued electrolyte absorption by the jejunum and ileum (2). It is only when the rate of exotoxin-induced electrolyte secretion exceeds the absorptive capacity of any given segment of gut that net electrolyte output occurs. Since, in canine studies, the rates of exotoxin-induced electrolyte secretion are not significantly different in jejunum and ileum, and the absorptive capacity per unit length of jejunum is less than that of ileum (2), the "lag period" in the ileum is greater than in the jejunum. If the above hypothesis is correct, there should be no significant lag period in the canine duodenum in which there is, under normal conditions, little or no net absorption of isotonic saline (6). The time of maximum fluid output by the duodenum should, however, be identical with that by jejunum and ileum. In the current studies, duodenal Thiry-Vella fistulae were employed to test the above hypothesis, to delineate more clearly the time of onset of action of the cholera exotoxin, and to define the response of the duodenum to challenge with cholera exotoxin.

METHODS

All studies were performed in adult mongrel dogs weighing 12–22 kg. Animals were fasted for 18 hr before each study. Sodium and potassium determinations were performed on a Patwin flame photometer with lithium internal standard (National Instrument Laboratories, Inc., Rockville, Md.). Carbon dioxide content was determined by a Natelson microgasometer (Scientific Industries, Inc., Springfield, Mass.). Reducing substances were determined by the technique of Hoffman (7) using the Technicon AutoAnalyzer (Technicon Corporation, Ardsley, N. Y.). Total proteins were determined by the Folin-Ciocalteu method (8). Phenolsulphonephthalein (PSP) was determined photometrically by the technique of Schedl and Clifton (9).

The crude cholera extoxin consisted of a 0.22 μ Millipore filtrate (Millipore Filter Corp., Bedford, Mass.) of a 48 hr stationary culture of *V. cholerae* Inaba, strain B1307, grown at 37°C in 2% Bactopeptone, as described by Craig (10). The crude filtrate was lyophilized and stored at 4°C until the week before its use in the canine studies. The lyophilized filtrate was then restored to an osmolarity of approximately 350 mOsm/liter by addition of 30 ml of distilled water/g of filtrate. The liquid filtrate was dialyzed and concentrated by pressure ultrafiltration through a Diaflo UM-1 membrane (Amicon Corp., Lexington, Mass.). The concentrate had a pH of 7.03 and an osmolarity of 16 mOsm/liter; sodium, potassium, and chloride were each present in concentrations of less than 1 mEq/liter. 5 ml of the concentrate (derived from 60 ml of filtrate) was used for each canine gut challenge.

The Thiry-Vella duodenal fistulae were made by dividing the second portion of duodenum 2–3 cm distal to the orifice of the common bile duct, dividing the proximal jejunum at center of the first mesenteric vascular arcade distal to the ligament of Treitz and exteriorizing both ends of the isolated duodenal loop. The proximal duodenal stump was directly anastomosed to the jejunum by serosa-to-serosa sutures. The lengths of the isolated duodenal loops, measured at the completion of the studies, varied from 18 to 38 cm. Thiry-Vella ileal loops were made by standard techniques, employing the distal 70 cm of ileum.

Experiment I (10 dogs) was designed to delineate the response of the duodenum to intraluminal challenge by crude cholera exotoxin. Each of the 10 isolated duodenal loops was challenged 2 wk after preparation of the loop. On the morning of study, each animal was lightly anesthetized with Nembutal, and Foley catheters were placed, with balloons inflated, in the proximal and distal orifices of the Thiry-Vella loops. The loops were gently flushed with 100 ml of air, and were then allowed to drain freely over the next 2 hr period. At the end of this time, the loops were again gently flushed with 100 ml of air, and the rate of fluid production was determined in those animals in which fluid output was observed. After this 2 hr control period, 5 ml of the exotoxin concentrate was placed in the loop via the proximal Foley catheter. Catheters were then clamped for the following 15 min period. After 15 min, both proximal and distal catheters were opened and allowed to drain into graduated cylinders. The loop was flushed with 100 ml of air at 15-min intervals during the 1st hr of study, at 30-min intervals during the 2nd hr, and at hourly intervals thereafter for 12 hr after challenge. Output volume was recorded for each collection period and electrolytes were determined on the fluid collected. Total protein concentration was determined on fluid collected during the 5th hr after challenge. Hematocrits were determined at 2-hr intervals, and intravenous fluids (two parts isotonic sodium chloride to one part 1/6 molar sodium lactate) were given at a rate sufficient to maintain a stable hematocrit. Plasma electrolytes were determined at the beginning and the end of each study.

Experiment II (seven dogs) was designed to test the hypothesis that the cholera exotoxin exerts an effect on electrolyte movement in the canine ileum shortly after its administration, and before net fluid production by exotoxin-challenged ileal loops is observed. All studies were performed 1–3 wk after construction of the ileal loops. On the day of study, each animal was lightly anesthetized with Nembutal, and Foley catheters were placed, with balloons inserted, in the proximal and distal orifices of the ileal loops. After flushing each loop with 200 ml of air, 150 ml of a solution containing sodium, 140 mEq/liter; potassium, 10 mEq/liter; chloride, 100 mEq/liter; and bicarbonate, 50 mEq/liter was placed in the ileal loop, and both proximal and distal catheters were

clamped shut. After 30 min, both catheters were opened and allowed to drain into a graduated cylinder, while the loop was gently flushed with 200 ml of air; the effluent volume was recorded. The same process was repeated for four successive 30-min periods, and the volume of fluid absorbed during each period was determined. Then 5 ml of the exotoxin concentrate and 145 ml of the above electrolyte solution were placed in the loop and both catheters were clamped shut. After 30 min, the catheters were opened and allowed to drain into a graduated cylinder while the loop was flushed with 200 ml of air. Then 150 ml of the above electrolyte solution was again placed in the loop and both catheters were clamped shut for the next 30-min period. The same process was repeated over consecutive 30-min periods, until the loop drainage exceeded 150 ml at the end of the period. From this time, both ends of the loop were allowed to drain freely into a graduated cylinder, and effluent measurements were made hourly after gentle flushing of the loop with 200 ml of air. The period of observation extended for 10 hr after exotoxin challenge.

Experiment III (nine dogs) was designed to determine the effect of intraluminal glucose on electrolyte movement in the duodenal loops before and after administration of cholera exotoxin. The experiments were performed, during the 3rd and 4th wk after preparation of the duodenal loops, in 9 of the 10 animals with chronic duodenal loops studied in experiment I. Each experiment consisted of two studies, each consisting of three periods. During the initial period (3 hr) of the first study, the bowel loop was perfused, at a rate of 10 ml/kg per hr, with an isotonic electrolyte solution containing the following solutes: sodium, 145 mEq/liter; potassium, 5 mEq/liter; chloride, 130 mEq/liter; and bicarbonate, 15 mEq/liter. At the end of this period the loop was gently flushed with 100 ml of air and the rate of absorption of the perfusion fluid was determined. The exotoxin concentrate was then placed in the loop, and proximal and distal catheters were clamped for the next hr. The catheters were then allowed to drain freely over the next hr, after which the loop was flushed with 100 ml of air and fluid output was recorded. The loop was then perfused with the same isotonic electrolyte solution for an additional 3 hr period, at the end of which time the loop was again flushed with 100 ml of air. The loop was then allowed to drain freely into a graduated cylinder over the next 2 hr period; the loop was then again flushed with 100 ml of air and the volume of fluid output was recorded.

1 wk after the first perfusion study, the second study was performed in the same dog, this time using a perfusion fluid containing: glucose, 60 mOsm/liter; sodium, 115 mEq/liter; potassium, 5 mEq/liter; chloride, 105 mEq/liter; and bicarbonate, 15 mEq/liter. In each study, net electrolyte absorption or secretion by the duodenal loop, before and after exotoxin administration, was determined. In four of the studies, PSP was added to the perfusion fluid in a concentration of 15 mg/100 ml, and recovery of PSP from the effluent was used to estimate the amount of residual fluid retained in the loops at the end of each 3 hr perfusion period.

RESULTS

Experiment I. In 3 of the 10 animals, the duodenal loops produced fluid at rates of 0.1–0.4 ml/cm per hr during the 2 hr period of control observations. In these animals, the control rate of fluid production was subtracted from the rate of fluid production during each interval after exotoxin administration in order to determine the rate of exotoxin-induced fluid output. All 10 duodenal loops responded to exotoxin challenge with production of isotonic fluid (Table I). In all studies, fluid output was observed during the 1st hr after exotoxin challenge (Table I). In each of the three animals in which fluid production occurred during the control period, the rate of fluid production during the 1st hr after exotoxin administration exceeded the rate observed during the control period. In 8 of the 10 studies, net fluid production was observed during the 1st 15 min after exotoxin challenge. (Net fluid production during the 1st 15 min was obtained by subtracting the 5 ml of administered exotoxin concentrate from the total exotoxin-induced fluid output during the 15 min period.) The mean fluid output increased at a nearly constant rate during the 1st 3 hr after exotoxin challenge (Tables I and II), and reached maximum values during the 4th and 5th hr after

TABLE I

Output of Isotonic Fluid during the 12 Hr Period Following Intraluminal Challenge of Thiry-Vella Duodenal Loops with Crude Cholera Exotoxin

Time after exotoxin challenge	Output volume
(*hr*)	(*ml/cm per hr*)
0– 1	0.5 ±0.4
1– 2	0.9 ±0.5
2– 3	1.4 ±0.6
3– 4	1.7 ±0.5
4– 5	1.7 ±0.5
5– 6	1.6 ±0.5
6– 7	1.6 ±0.4
7– 8	1.5 ±0.4
8– 9	1.5 ±0.5
9–10	1.4 ±0.5
10–11	1.3 ±0.5
11–12	1.1 ±0.3

Mean values ±SD, 10 dogs.

TABLE II

Output of Isotonic Fluid at 30-Min Intervals during the 1st 2 Hr Period after Intraluminal Challenge of Duodenal Loops with Crude Cholera Exotoxin

Time after exotoxin challenge	Output volume
min	*ml/cm*
0– 30	0.19 (0–0.54)
30– 60	0.28 (0.06–0.54)
60– 90	0.36 (0.08–0.75)
90–120	0.57 (0.27–1.10)

Mean values, 10 dogs (ranges in parentheses).

challenge. The mean rate of fluid production was sustained at nearly maximum values through the 9th hr after challenge and then showed a very gradual decrease during the remainder of the period of observation (Table I). In all animals, detectable fluid production continued for 24–36 hr after challenge.

Table III shows the electrolyte pattern of the duodenal fluid produced during the 5th hr after exotoxin challenge. The electrolyte concentrations of the duodenal fluid remained essentially unchanged throughout each 12 hr period of study in a given animal. No significant changes in plasma electrolytes occurred during these studies. The mean total protein concentration of the duodenal fluid was 303 ±203 (SD) mg/100 ml; this value does not differ significantly from values previously observed in fluid produced by exotoxin-challenged jejunal and ileal loops (2).

Experiment II. All ileal loops demonstrated net absorption of the administered isotonic intraluminal fluid during each of the four 30 min control periods. Mean rate of isotonic fluid absorption during this period was 1.35 ml/cm per hr (Table IV). In six of the seven studies, a decreased rate of isotonic fluid absorption was observed during the 1st hr after exotoxin administration; the mean rate of absorption during this period was 1.0 ±0.7 (SD) ml/cm per hr. A further decrease in mean rate of absorption occurred during the 2nd hr after exotoxin administration (Table IV).

During the 3rd hr after exotoxin administration, net secretion of isotonic fluid was observed in five of the seven studies, and the animals exhibited a mean net isotonic fluid secretion of 0.2 ±0.2 (SD) ml/cm per hr during this period. The mean rates of isotonic fluid output reached levels of 0.6 and 0.7 ml/cm per hr during the 4th and 5th hr after challenge, respectively. The mean rates of fluid output then remained at maximal levels through the 10th hr after challenge (Table IV). The rate of fluid output then decreased gradually, and generally ceased entirely within less than 24 hr after exotoxin administration.

The mean electrolyte composition of the isotonic fluid drained from the ileal loops at the end of each of the 30-min control periods differed significantly from that placed in the loops at the beginning of the periods. The mean chloride concentration had decreased to 76 ±9 (SD) mEq/liter; bicarbonate concentration had increased to 65 ±4 (SD) mEq/liter; potassium concentration had decreased to 7.9 ±1.4 (SD) mEq/liter; and

TABLE III

Electrolyte Values of Duodenal Fluid Produced in Response to Intraluminal Challenge with Crude Cholera Exotoxin

	mEq/liter
Sodium	140 ±10
Chloride	118 ±10
Potassium	5.9 ±1.1
Bicarbonate	24 ±6

Mean values ±SD of fluid produced during the 5th hr after exotoxin challenge in 10 dogs.

TABLE IV

Net Isotonic Fluid Absorption (+) or Secretion (−) by Chronic Canine Ileal Loops before and after Administration of Crude Cholera Exotoxin

Time before (−) and after administration of exotoxin	Volume of fluid absorbed (+) or secreted (−)
hr	*ml/cm per hr*
−2– −1	+1.4 ±0.7
−1– 0	+1.3 ±0.9
0– 1	+1.0 ±0.7
1– 2	+0.5 ±0.6
2– 3	−0.2 ±0.2
3– 4	−0.6 ±0.4
4– 5	−0.7 ±0.2
5– 6	−0.7 ±0.3
6– 7	−0.8 ±0.3
7– 8	−0.7 ±0.3
8– 9	−0.8 ±0.3
9– 10	−0.7 ±0.3

Mean values ±SD, seven dogs.

mean sodium concentration had not changed significantly. The fluid produced by the ileal loops during the 5th hr after exotoxin administration showed the following electrolyte concentrations (mean values ±SD): sodium, 137 ±14 mEq/liter; potassium, 7.2 ±2.5 mEq/liter; chloride, 76 ±4 mEq/liter; bicarbonate, 66 ±5 mEq/liter. The electrolyte pattern of the ileal fluid produced in response to exotoxin challenge was essentially the same as that of the fluid obtained from the ileal loops during the control periods.

Experiment III. During control perfusion with isotonic fluid containing no glucose, net fluid absorption was observed in six and net production in three experiments. Mean isotonic fluid absorption of 0.2 ml/cm per hr was observed during this period (Table V). Within 1 hr after exotoxin administration, output of isotonic fluid was observed in all loops. During the perfusion period after exotoxin administration, all animals exhibited continued fluid and electrolyte loss. The mean net secretion of isotonic fluid during this period was 2.1 ml/cm per hr. The mean rate of isotonic fluid output from the loops during the 2 hr period after cessation of perfusion was 1.9 ± 0.6 (SD) ml/cm per hr.

When the perfusion fluid contained glucose, 60 mOsm/liter, isotonic fluid absorption was observed during the control period in every animal. The mean rate of absorption of perfusion fluid was 1.5 ±0.9 (SD) ml/cm per hr (Table V); this value is significantly greater than the rate observed during the control period when the perfusion fluid contained no glucose ($t = 3.27$, $P < 0.01$). In each study, net production of isotonic fluid occurred within 1 hr after intraluminal administration of cholera exotoxin. During the postexotoxin glucose perfusion period, all animals continued to exhibit net isotonic fluid loss. The mean rate of net gut fluid secretion was 1.3 ±0.6 (SD) ml/cm per hr, which is significantly less than the rate observed during perfusion by the nonglucose-containing solution ($t = 2.13$, $P < 0.05$). The mean rate of isotonic fluid output during the 2 hr period after cessation of perfusion was 1.8 ±0.5 (SD) ml/cm per hr. This value is virtually identical to the rate of fluid output observed during the 2 hr period after cessation of perfusion with the nonglucose-containing solution.

The net effect of exotoxin on isotonic fluid movement was not significantly different during perfusion studies with glucose from that observed during perfusion with isotonic fluid containing no glucose. The mean net effect of the exotoxin was to increase secretion (or decrease absorption) by 2.3 ml/cm per hr during perfusion studies without glucose and by 2.8 ml/cm per hr during studies with glucose. Conversely, the effect of glucose in increasing isotonic fluid absorption was not significantly altered by exotoxin administration. The mean net effect of glucose was to increase isotonic fluid absorption by 1.3 ml/cm per hr in control loops and by 0.8 ml/cm per hr in exotoxin-treated loops.

Glucose was absorbed from the perfusate in all studies. The rate of glucose absorption during the postexotoxin perfusion period, 17 ±6 (SD) mg/cm per hr, was not significantly different from the rate of 26 ±7 (SD) mg/cm per hr during the control period.

In the four studies in which PSP, 15 mg/100 ml, was added to the perfusate as a nonabsorbable marker, from 87 to 97% of administered PSP was recovered from the loop effluent at the end of each perfusion period.

During the perfusion studies without glucose, the isotonic perfusion fluid showed no significant alterations in electrolyte concentrations during passage through the loops, either before or after exotoxin administration. During perfusion with glucose-containing solution, the mean glucose concentration of the perfusate consistently decreased and the mean sodium concentration increased during passage through the loops, both before and after exotoxin administration. Mean glucose concentrations of the perfusate were 736 ±125 (SD) mg/100 ml and 641 ±112 (SD) mg/100 ml after passage through control and

TABLE V

Net Absorption (+) or (−) Secretion of Isotonic Fluid During Perfusion of Duodenal Loops before and after Intraluminal Administration of Cholera Exotoxin

	Control	After exotoxin
	ml/cm per hr	*ml/cm per hr*
Perfusion fluid with no glucose	+0.2 ±0.6	−2.1 ±0.9
Perfusion fluid containing glucose, 60 mOsm/liter	+1.5 ±0.9	−1.3 ±0.6

Mean values ±SD, nine dogs.

exotoxin-treated loops, respectively. Mean sodium concentrations of the perfusate were 121 ±6 (SD) mEq/liter and 128 ±8 (SD) mEq/liter after passage through control and exotoxin-treated loops, respectively. Other perfusate electrolytes were not significantly altered during the studies. Mean plasma electrolyte values remained within normal limits throughout the studies.

DISCUSSION

The current data indicate that net production of isotonic fluid by canine duodenal loops may be seen within 15 min after intraluminal administration of crude cholera exotoxin, and that the maximum rate of exotoxin-induced fluid production is reached 4–5 hr after exotoxin administration. Earlier investigations in the rabbit ileal loop had suggested that a "latent period" of approximately 4 hr occurred between exotoxin administration and net fluid production in that model (11). Subsequent studies in the dog demonstrated that net fluid production by jejunal loops began during the 2nd hr after exotoxin administration, while net fluid output by ileal loops was not observed until the 3rd hr after exotoxin challenge (2). The earlier canine studies were consistent with the hypothesis that increased secretion of isotonic fluid began shortly after exotoxin administration in both jejunal and ileal loops, but that *net* fluid production was not observed until the absorptive capacities of the respective loops were exceeded; the greater time lag in the ileal loops resulted from the greater absorptive capacity of the ileal loops. The current studies are entirely consistent with this hypothesis, as net fluid production by duodenal loops, which normally exhibit little or no absorption of isotonic saline (6), generally began within 15 min after intraluminal exotoxin administration; and the time at which maximal fluid production occurred was the same in all segments of small bowel studied.

The previous studies in the dog demonstrated that the mean rate of exotoxin-induced fluid production by jejunal loops was significantly greater, per unit length, than that by ileal loops. The data suggested that the greater net fluid production by jejunal loops resulted from the lesser absorptive capacity of the jejunal loops (2). If this hypothesis is applied to duodenal loops, a still greater net isotonic fluid production per unit length would be expected, since canine duodenal loops exhibit very little absorption of isotonic intraluminal saline. The current studies demonstrate that this is indeed the case. The mean hourly rate of isotonic fluid output during the period of maximal fluid production (4–8 hr after exotoxin challenge) was 1.7 ±0.5 (SD) ml/cm for duodenal loops, as compared to previously observed values of 1.4 ±0.2 (SD) ml/cm and 0.7 ±0.3 (SD) ml/cm for jejunal and ileal loops, respectively (2).

Isotope studies have indicated that lumen-to-plasma flux of sodium is not altered following intraluminal administration of cholera exotoxin to rabbit (4) or canine (5) small bowel loops. The exotoxin-induced plasma-to-lumen movement of isotonic fluid by a small bowel segment should, therefore, equal the sum of the absorptive capacity for isotonic fluid of that segment, plus the net fluid secretion by that segment. In previously described perfusion studies, mean absorptive capacities of canine jejunal and ileal loops were, respectively, 0.7 ±0.4 and 1.0 ±0.3 ml/cm per hr; the mean rates of exotoxin-induced plasma-to-lumen movement (net secretion plus normal absorption) of isotonic fluid by jejunal and ileal loops were, respectively, 2.1 ml/cm per hr and 1.9 ml/cm per hr (2) during the period of maximum exotoxin effect. The mean absorptive capacity for duodenal loops, observed in the current, similarly designed perfusion studies, was 0.2 ±0.6 ml/cm per hr; the mean rate of exotoxin-induced plasma-to-lumen movement (net secretion plus normal absorption) of isotonic fluid by the duodenal loops was 2.3 ml/cm per hr (Table V). These data suggest that the rate of exotoxin-induced plasma-to-lumen movement of isotonic fluid is roughly equal in all segments of the small gut (Fig. 1). Although the exotoxin causes a greater *net* secretion of isotonic fluid in duodenum than in the more distal small bowel segments, the major reason for the greater net fluid output by duodenal, as compared with that of jejunal and ileal loops, appears to be that the more distal segments absorb isotonic intraluminal fluid at a greater rate.

Intraluminal glucose enhances isotonic fluid absorption during perfusion of duodenal loops by an isotonic electrolyte solution. In the current duodenal studies, the glucose-associated enhancement of isotonic fluid absorption per unit length of small bowel was not significantly different from

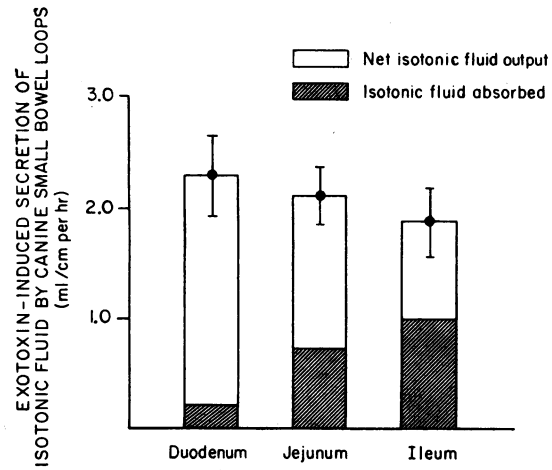

FIGURE 1 Exotoxin-induced isotonic fluid secretion by canine Thiry-Vella small bowel loops during period of maximal exotoxin effect on isotonic fluid movement (see text). Values for duodenal loops are obtained from experiment III of the current study. Values for jejunal and ileal loops are from previously reported investigations (2). Bars represent mean exotoxin-induced isotonic fluid secretion for nine duodenal, six jejunal, and six ileal loops, respectively. Brackets indicate 95% confidence limits of the means.

that observed in earlier studies of canine jejunal and ileal loops (2). The current data are consistent with the earlier observations in jejunal and ileal loops in indicating that intraluminal glucose does not significantly alter the effect of cholera exotoxin in the canine gut; the effect of exotoxin in increasing isotonic fluid secretion in the presence of intraluminal glucose was not detectably different from its effect in the absence of glucose. Conversely, the effect of glucose in enhancing isotonic fluid absorption was not significantly different in control and exotoxin-treated duodenal loops.

The observed responses of the ileal loops in the current studies indicate that, as with duodenal loops, the exotoxin leads to increased secretion of isotonic fluid very shortly after administration, and the rate of exotoxin-induced electrolyte secretion increases progressively over the 1st 4 hr after its administration (Fig. 2). Net fluid production fails to occur in ileal loops until the rate of exotoxin-induced isotonic fluid secretion exceeds the absorptive capacity of the loop (Fig. 2). In the current investigations, the rates of isotonic fluid absorption during the control period and of isotonic fluid production after exotoxin administration are similar to the rates observed in previous studies of the response of ileal loops to cholera exotoxin (2).

Although times of onset of net fluid production were significantly different in duodenal and ileal loops, the slopes of the curves describing the exotoxin-induced fluid production in the two small bowel segments were virtually identical (Fig. 2). The ileal loops exhibited essentially the same pattern of response as the duodenal loops. In both duodenal and ileal loops, the exotoxin-induced plasma-to-lumen movement of isotonic fluid began within 30 min after exotoxin administration, increased

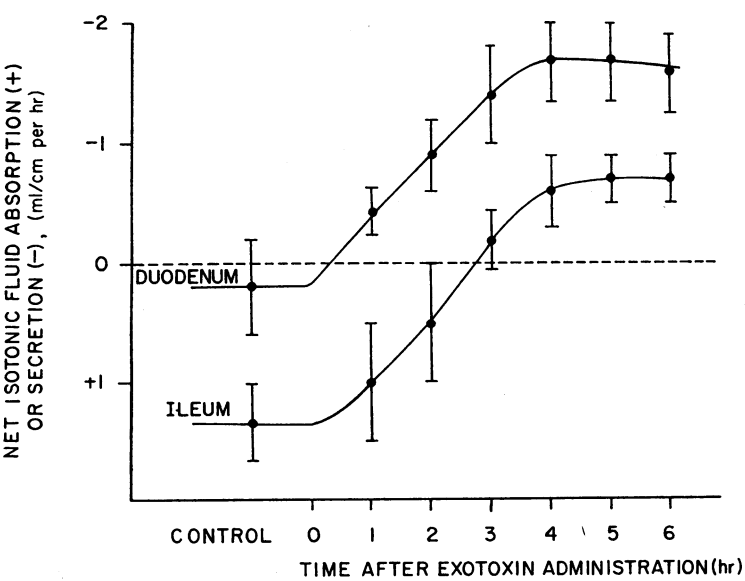

FIGURE 2 Net isotonic fluid absorption (+) or secretion (−) by Thiry-Vella duodenal and ileal loops before and after intraluminal administration of cholera exotoxin. Values for ileal loops are obtained from experiment II. For duodenal loops, control values are obtained from experiment III, postexotoxin values are obtained from experiment I. Lines are hand-fitted to experimental points. Brackets indicate 95% confidence limits of the mean values.

progressively over the initial 4 hr (Fig. 2), then showed little change over the subsequent 6 hr period. Net isotonic fluid output by both duodenal and ileal loops then gradually decreased, but net fluid production by duodenal loops persisted for 6–12 hr longer than net fluid production by ileal loops. Both the time of onset of exotoxin effect and the time at which maximal rates of secretion were reached were essentially the same in all segments of the small gut. The reason for delay in reaching maximal exotoxin-induced secretion rates is not known.

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