January 1986
Volume 203, Number 1

Annals of Surgery

Effects of Bombesin on Fasting Bile Formation

WARREN J. KORTZ, M.D. JAMES R. B. NASHOLD, B.S. ELIZABETH DELONG, PH.D. WILLIAM C. MEYERS, M.D.

From the Department of Surgery, Duke University Medical Center, Veterans Administration Medical Center, Durham, North Carolina

Adult dogs were previously prepared by cholecystectomy, ligation of the lesser pancreatic duct, and insertion of cannulae into the duodenum and stomach. After a 2-week period of postoperative recovery and an overnight fast, bile ducts were cannulated, gastric cannulae placed to open drainage and sodium taurocholate 500 mg hr^{-1} was administered to replace bile acids lost from the interrupted enterohepatic circuit. Bombesin was infused IV for 1 hour over the dose range, 0.625–10 ng kg^{-1} min^{-1}. In control experiments 0.15 N NaCl was infused. Bombesin caused a significant increase in fasting bile flow, 3.0 ± 0.2 ml/15 min to 4.2 ± 0.3 ml/15 min (40%). Bile acid and phospholipid outputs were unchanged during bombesin. Bile cholesterol output decreased significantly during bombesin, 1029 ± 142 μg/15 min to 856 ± 109 μg/15 min (17%). The increase in bile flow was linearly related to the logarithm of the bombesin dose. In dogs with pyloric occlusion, to prevent acid from reaching the duodenum, bombesin increased bile flow and bicarbonate output but had no effect on ^{14}C erythritol biliary clearance. Bombesin stimulated ductular bile acid independent bile formation in a dose-dependent manner. Bombesin also inhibited bile cholesterol output.

BOMBESIN, a tetradecapeptide initially isolated from the skin of the discoglossidae frog *Bombina bombina,*[1] has profound effects on gastrointestinal function. Bombesin is a potent stimulator of gastrin release.[2,3] The increase in gastric acid secretion following bombesin is thought secondary to this gastrin release but may be secondary to a direct effect of bombesin on gastric mucosa.[4] Bombesin causes increased plasma levels of cholecystokinin (CCK),[5] and the stimulatory effects of bombesin on gallbladder contractility and pancreatic protein secretion may be *via* this CCK release[6] but again may occur *via* a direct effect of bombesin on target organs.[7] Bombesin also stimulates the release of a variety of other gastrointestinal peptides: GIP, pancreatic polypeptide, somatostatin, insulin, glucagon, enteroglucagon, motilin, and neurotensin.[8–13]

There is evidence that bombesin-like peptides with similar structure and effects are important in mammalian gastrointestinal function. A 27-amino acid peptide has been isolated from porcine intestinal mucosa, gastrin-releasing-peptide (GRP), which has a carboxy-terminal sequence similar to bombesin.[14] Bombesin-like immunoreactivity is present in the human gastrointestinal tract.[15] Recently, two bombesin-like peptides have been isolated from the canine intestinal tract; one peptide is 27 amino acids in length and similar to porcine GRP, and the other peptide, 10 amino acids in size, is similar to frog bombesin.[16]

Address for correspondence: Warren J. Kortz, M.D., Box 3908, Duke University Medical Center, Durham, NC 27710.

Submitted for publication: August 19, 1985.

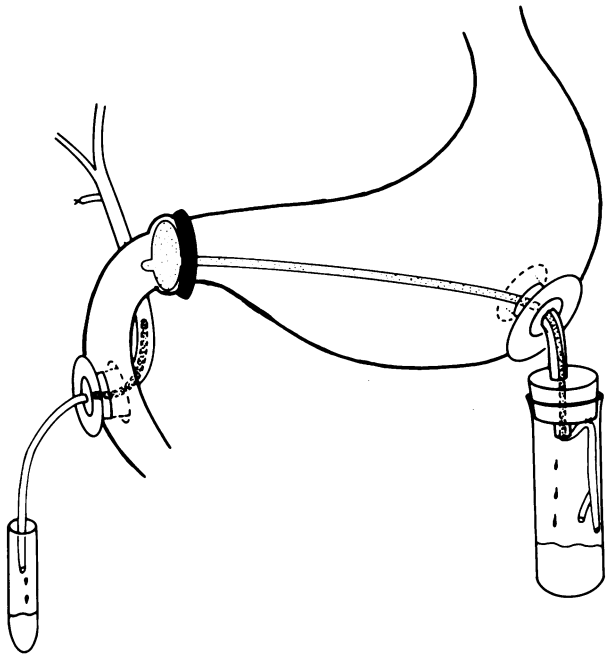

FIG. 1. Diagram of the pyloric occlusion model, showing bile and gastric drainage.

Previously observed effects of bombesin on biliary function are thought secondary to gallbladder contraction mediated through CCK release. The one study examining the effect of bombesin on hepatic bile formation in cholecystectomized dogs revealed no changes in fasting, unstimulated bile secretion.[17] We have further studied the effects of bombesin on fasting canine hepatic bile formation.

Methods

Adult mongrel dogs (15–22 kg) were anesthetized with sodium pentobarbital (30 mg/kg) and underwent cholecystectomy, ligation of the lesser pancreatic duct, insertion of modified Thomas cannulae into the stomach and duodenum,[18] and placement of a circumferential 0.5 cm band of Dacron® graft sewn loosely around the pylorus. After operation, the animals recovered for 2 weeks prior to study.

The animals were fasted except for water 18 hours prior to study. After gently restraining the animals in slings, 0.15 N NaCl was administered intravenously at 50 ml hr^{-1} using a Harvard peristaltic pump. The common bile duct was cannulated with a #6 F ureteral catheter placed through a cork used to occlude the duodenal cannula. Gastric cannulae were opened and gastric secretions collected. After one hour of saline, sodium taurocholate (CalBiochem) 500 mg hr^{-1} was infused I.V. to replace bile acids lost to the interrupted enterohepatic circuit. At the end of the third hour, either bombesin (Sigma Chemical Co., St. Louis, MO) or 0.15 N NaCl was infused for 1 hour with a Harvard peristaltic pump. Five animals were studied twice with each dose of bombesin, 0.625, 1.25, 2.5, 5.0, and 10.0 ng kg^{-1} min^{-1}, or saline. In addition, five animals were studied twice with CCK-8 (sincalide), 2 ng kg^{-1} min^{-1}, for 1 hour using the same protocol described above. Animals were studied no more frequently than twice per week.

Bile was collected every 15 minutes, measured to the nearest 0.1 ml and frozen for later analysis. Bile acid concentrations were measured using a steroid dehydrogenase method.[19] Bile cholesterol was estimated using the method of Abel[20] and bile phospholipid content measured according to Fiske.[21] Gastric secretions were collected every 30 minutes and measured to the nearest 1.0 ml. One-half ml of gastric secretion was titrated to a pH of 7.0 using 0.2 N NaOH and a radiometer automatic titrator. Gastric acid output was calculated by multiplying the 30 minute volume times the H^+ concentration (mEq/ml).

Blood samples were drawn from a peripheral vein, centrifuged and plasma glucose determined with a glucose-oxidase method (Beckman). In addition, plasma was frozen with Trasylol® (Sigma) for future analysis of glucagon and insulin concentrations using standard radioimmunoassay techniques.

Pyloric Occlusion

Since bombesin stimulated gastric acid output, additional studies were performed with pyloric occlusion (Fig. 1). These experiments were performed to exclude the possibility that hormonal release secondary to duodenal acidification despite open gastric drainage was responsible for the changes in bile production detected during bombesin infusion. A #12 F Foley was introduced through the gastric cannula and placed through the pylorus. The Foley balloon was inflated and traction placed on the catheter to occlude the pylorus against the buttress created by the previously placed external Dacron® cuff. Pyloric occlusion was confirmed by radiographic barium examination. The Foley catheter was secured to the gastric cannula and collection of gastric secretion was identical to that described above. Five animals were studied twice each with bombesin, 5 ng kg^{-1} min^{-1}, or 0.15 N NaCl in a manner similar to above experiments. In addition, ^{14}C erythritol, 3 μCi, was given as an I.V. bolus and then infused intravenously 3 μCi hr^{-1} for the duration of the experiment. ^{14}C activity was measured in bile and serum and ^{14}C erythritol biliary clearance determined, as previously described.[22] Bile bicarbonate and bile chloride concentrations of fresh bile samples were measured using an Astra 8, Beckman Instrument.

Data is expressed as the mean ± standard error of the mean. Statistical analysis was performed using the Stu-

dent's t-test for paired data. Differences were considered significant if $p < 0.05$. In addition, we performed a linear regression analysis to determine whether the value of bile flow obtained at the end of test substance infusion, 15-minute period 16 (P16), was dose related using the preinfusion period 12 (P12) as baseline. The serial dilutions of dosage were first converted to a logarithmic scale by setting the control experiment at zero and letting higher bombesin doses (0.625, 1.25, . . . 10.0) correspond to higher converted doses (1, 2, . . . 5). To account for repeated measurements on individual dogs, a random dog effect was included in the model. Nonhomogeneity of slopes over dogs and nonlinearity of the response as a function of converted dose level were tested in the model and found to be insignificant. The analysis modeled the P16 value for bile flow as a function of the baseline value and the converted dose level, with a different intercept term for each dog. Scatterplots of residuals indicated no departures from the assumptions of the model.

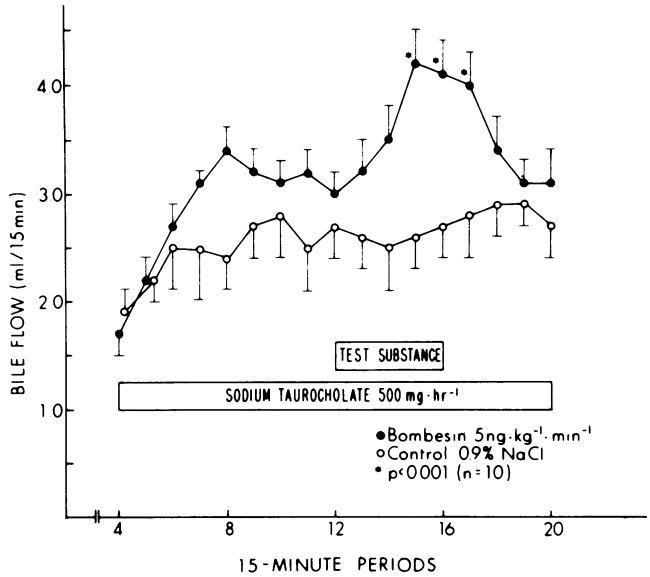

FIG. 2. Effects of bombesin or saline on fasting bile flow. Asterisk denotes a significant ($p < 0.001$) increase in bile flow compared to baseline period 12.

Results

As shown in Figure 2, bombesin 5 ng kg^{-1} min^{-1} for 1 hour caused a significant increase in bile flow, comparing baseline period 12, 3.0 ± 0.2 ml/15 min, to period 15, 4.2 ± 0.3 ml/15 min, and period 16, 4.1 ± 0.3 ml/15 min. The increase in bile flow remained significantly greater than baseline for 15 minutes after cessation of bombesin, but by 30 minutes postinfusion bile flow was no longer elevated. Bile flow during control experiments was stable.

Table 1 demonstrates the effects on bile acid, bile cholesterol, and bile phospholipid during bombesin, 5 ng kg^{-1} min^{-1} and control 0.15 N NaCl. Bile acid, cholesterol, and phospholipid concentrations decreased significantly during bombesin. These measurements were unchanged during control experiments. The decreases in bile and phospholipid concentration were offset by the simultaneous increase in bile production during bombesin, so that bile acid and bile phospholipid outputs were unchanged. However, cholesterol output decreased significantly during bombesin when compared to baseline period 12, while the same measurement was unchanged in control experiments. The effects on bile cholesterol are shown in more detail in Figure 3. The decrease in cholesterol output was still evident 30 minutes after termination of bombesin, but, by 1 hour postinfusion, cholesterol output had returned to baseline values. Significant decreases in cholesterol output were also observed for bombesin 1.25 and 2.5 ng kg^{-1} min^{-1} (Table 2). Since bombesin stimulates the release of cholecystokinin, studies were performed to examine the effects of CCK-8 on bile cholesterol output. CCK-8 produced a significant increase in bile flow during period 16, 3.8 ± 0.2 ml/15 min, when compared to baseline period 12, 3.1 ± 0.2 ml/15 min. Bile cholesterol output in these experiments was not affected significantly (937 ± 83 μg/15 min to 883 ± 86 μg/15 min).

Bombesin 5 ng kg^{-1} min^{-1} caused a significant increase in gastric acid output that was maximal during the 30 minutes postinfusion, 2.20 ± 0.87 mEq/30 min ($p < 0.05$),

TABLE 1. *Effects of Bombesin on Bile Composition*

Bile Analysis (N = 10)	Bombesin (5 ng kg^{-1} min^{-1})		0.15 N NaCl	
	Per 12	Per 16	Per 12	Per 16
Bile acid conc. (mg/ml)	42.6 ± 2.1	34.6 ± 1.7*	50.7 ± 8.7	55.7 ± 7.2
Bile acid output (mg/15 min)	131 ± 10	139 ± 8	120 ± 19	146 ± 14
Cholesterol conc. (μg/ml)	346 ± 52	213 ± 24*	364 ± 39	412 ± 75
Cholesterol output (μg/15 min)	1029 ± 142	856 ± 109*	958 ± 102	981 ± 94
Phospholipid conc. (mg/ml)	10.8 ± 1.3	8.1 ± 0.7*	10.0 ± 1.0	9.7 ± 1.3
Phospholipid output (mg/15 min)	31.8 ± 3.1	31.9 ± 2.4	27.7 ± 3.7	25.2 ± 3.6

* $p < 0.025$ compared to baseline period 12.

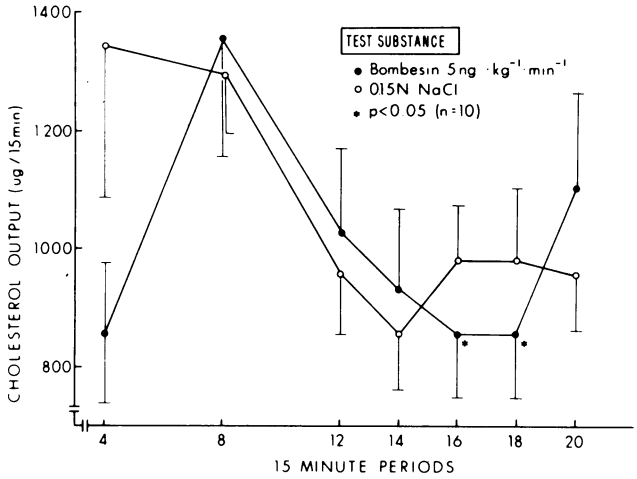

FIG. 3. Effects of bombesin or saline on bile cholesterol output. Asterisk denotes a significant ($p < 0.05$) decrease in bile cholesterol output compared to baseline period 12.

when compared to baseline gastric acid output, 0.14 ± 0.07 mEq/30 min. Gastric acid output during control experiments was unchanged.

Table 3 lists the values for plasma glucose, glucagon, and insulin during bombesin 5 ng kg^{-1} min^{-1} or 0.15 N NaCl. Plasma glucagon increased significantly during bombesin, while plasma insulin and glucose were unchanged. Plasma glucose, glucagon, and insulin were stable during control experiments.

Figure 4 demonstrates that a significant increase in bile flow during bombesin also occurred in the setting of pyloric occlusion and gastric drainage. Again, this stimulation was short-lived, for bile flow returned to baseline values within 30 minutes postinfusion. Since secretin produces increases in bile bicarbonate output and small changes in ^{14}C erythritol biliary clearance, these parameters were measured in the pyloric occluded model to minimize the effect of duodenal acidification induced secretin release. Table 4 shows that bombesin 5 ng kg^{-1} min^{-1} for 1 hour caused a significant increase in bile bicarbonate output and bile chloride output. The small increase in ^{14}C erythritol biliary clearance was not statistically significant. Values measured during control experiments with pyloric occlusion showed no significant changes.

TABLE 2. *Effects of Lower Dose Bombesin on Cholesterol Output*

	Cholesterol Output (μg/15 min)	
	Period 12	Period 16
0.9% NaCl	958 ± 102	981 ± 94
Bombesin		
2.5 ng kg^{-1} min^{-1}	817 ± 101	692 ± 96*
1.25 ng kg^{-1} min^{-1}	1131 ± 167	873 ± 95*

* $p < 0.025$ compared to period 12.

The regression analysis performed to detect a relation between the bombesin dose infused and the change in bile flow yielded a statistically significant ($p < 0.001$) linear relation between P16 and the converted dose level, after adjusting for baseline value. The equation can be expressed as:

$$P16 - 0.885(P12) = INT_{dog} + 0.259(CDL),$$

where INT_{dog} is an intercept that is dog specific, and CDL is the converted dose level (0.625, 1.25, . . . 10.0 ng kg^{-1} min^{-1} = 1, 2, . . . 5). The dog effect in the intercept term was not significant ($p = 0.07$). Therefore, although the equations for different dogs are characterized by equations with different intercepts, the relation between P16 and the logarithm of dose level after adjusting for P12 remains linear with the same slope for all dogs. The R^2 for this model was 0.65. Figure 5 shows the data used to derive the above equation and the mean function of all dogs at all doses.

Discussion

Bombesin is one of the newer polypeptides shown to have a variety of effects on gastrointestinal function. Am-

TABLE 3. *Effects of Bombesin on Plasma Glucose, Glucagon, and Insulin (N = 10)*

15 Minute Periods	Bombesin (5 ng kg^{-1} min^{-1})				0.15 N NaCl			
	12	14	16	18	12	14	16	18
Plasma glucose (mg%)	88 ± 3	88 ± 4	90 ± 4	89 ± 2	91 ± 3	87 ± 3	89 ± 3	87 ± 3
Plasma glucagon (pg/ml)	57 ± 9	127 ± 20*	173 ± 18*	120 ± 17*	101 ± 18	97 ± 13	113 ± 25	93 ± 16
Plasma insulin (μU/ml)	20 ± 5	27 ± 8	15 ± 2	25 ± 6	19 ± 5	17 ± 4	23 ± 9	17 ± 4

* $p < 0.001$ compared to period 12.

phibian bombesin is a releaser of many other gastrointestinal peptides in various mammalian species. Gastrin, cholecystokinin, pancreatic polypeptide, glucagon, insulin, GIP, enteroglucagon, motilin, neurotensin, and somatostatin all increase with bombesin.[8–13] Bombesin also causes increased gastric acid output, pancreatic protein output, and gallbladder contractility. These effects may occur indirectly *via* hormone release or *via* direct actions on target organs. We investigated the effects of bombesin on bile secretion and have demonstrated a stimulatory effect on hepatic bile production and an inhibition of biliary cholesterol output.

Since bile acid output was stable, bombesin increased the bile acid independent fraction of bile production. Bombesin increased gastric acid output in these studies, so it was possible that bombesin choleresis occurred as a result of secretin release secondary to duodenal acidification. A previous study demonstrated that dependent gastric cannula drainge did not totally prevent histamine stimulated gastric acid from entering the duodenum.[23] We, therefore, repeated our studies during pyloric occlusion as documented by radiographic barium examination and have demonstrated that bombesin choleresis still occurred. Therefore, bombesin choleresis does not occur *via* the mechanism of duodenal acidification.

Bile bicarbonate output increased during bombesin. Secretion of biliary bicarbonate is a property of ductular epithelium, suggesting that bombesin affects the ductular portion of bile acid independent bile formation.[24,25] This is confirmed by the observation that significant changes in ^{14}C erythritol clearance, primarily a canalicular event, were not detected during bombesin. Small increases in ^{14}C erythritol clearance have been detected during infusion of the ductular stimulant secretin.[26,27] Experimental observations greater than the number used in our experiments with bombesin might reveal a similar significant increase in ^{14}C erythritol clearance.

The mechanism by which bombesin stimulates ductular bile formation is unknown. Bombesin stimulates the release of cholecystokinin, a known ductular stimulant

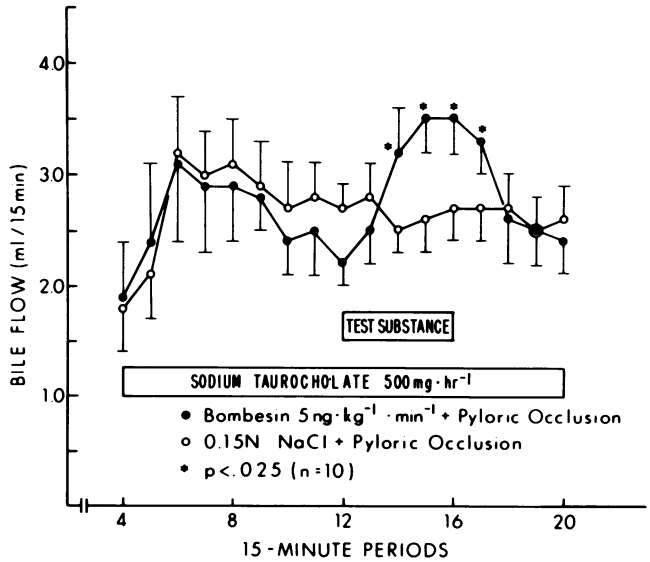

FIG. 4. Effects of bombesin or saline on bile flow in the setting of complete pyloric occlusion. Asterisk denotes a significant ($p < 0.025$) increase in bile flow compared to baseline period 12.

raising the possibility that bombesin increases hepatic bile production indirectly *via* CCK release. Bombesin could also affect bile formation *via* the release of other known ductular choleretics, *i.e.*, secretin; but one study showed no effect on secretin levels with bombesin.[28] Additional studies in isolated perfused systems will help to determine whether bombesin affects bile secretion *via* a direct mechanism.

Kaminski and Deshpande found no effects of bombesin on fasting bile formation using a similar chronic bile fistula model.[17] Their smallest dose of 83 ng kg^{-1} min^{-1} was eight times the largest dose used in the present studies. At larger doses, bombesin may produce offsetting choleretic and cholestatic effects or have no effect at all.

Bile cholesterol output was inhibited during bombesin. This effect occurred in the absence of changes in bile acid secretion or phospholipid output. We have shown previously that physiologic levels of glucagon lower biliary

TABLE 4. *Effects of Bombesin on Bile Bicarbonate, Chloride, and ^{14}C Erythritol Clearance*

	Bombesin Infusion (5 ng kg^{-1} min^{-1})		0.15 N NaCl Infusion	
	Pre Per 12	Post Per 16	Pre Per 12	Post Per 16
Bile HCO_3^- output (μmol/15 min, N = 8)	59.4 ± 18.5	135.3 ± 14.7*	59.8 ± 20.8	74.3 ± 17.8
Bile Cl^- output (μmol/15 min, N = 8)	169.8 ± 36.6	303.7 ± 45.9*	188.7 ± 45.5	190.8 ± 43.7
^{14}C erythritol clearance (ml/15 min, N = 10)	2.13 ± 0.14	2.81 ± 0.46	2.37 ± 0.16	2.1 ± 0.21

* $p < 0.005$ compared to period 12.

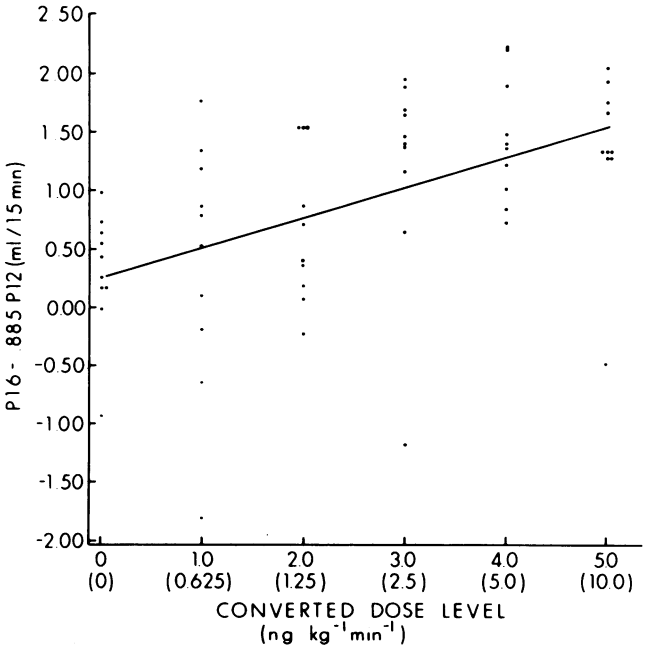

FIG. 5. The relation between log bombesin dose and bile flow demonstrated by the equation: P16 − 0.885 P12 = INT_{dog} + 0.259 (CDL).

cholesterol secretion.[29] Bombesin 5 ng kg^{-1} min^{-1} caused physiologic increases in plasma glucagon, suggesting that bombesin affects bile cholesterol output indirectly *via* glucagon release. Another mechanism, such as a direct inhibitory effect of bombesin on cholesterol secretion, was not excluded.

Plasma insulin and glucose were not significantly altered by bombesin. Others have shown stimulation of insulin release with bombesin.[30,31] In those studies, insulin increased within 10 minutes after bombesin infusion and then returned quickly to baseline levels. We drew samples every 30 minutes, past the time frame of these reported increases in insulin.

The relation between the bombesin dose and the response in bile flow was linear when the dose was corrected in a logarithmic fashion. The lowest bombesin dose that significantly increased bile flow was 1.25 ng kg^{-1} min^{-1}. Plasma bombesin levels were not measured in these experiments. It is not clear what levels of bombesin can be termed physiologic, since there were no increases in plasma bombesin detected in healthy volunteers after a standard meal.[32] There was one report of increased bombesin levels following a meal in human subjects, but little data were presented.[33] Bombesin is present in cells contained within the intestinal mucosa[34] and also within nerves of the myenteric plexus and submucosa.[35] It is possible that bombesin affects gastrointestinal physiology in a paracrine fashion or through neural influences totally independent of changes in circulating plasma levels of bombesin.

In summary, bombesin stimulates bile acid independent bile secretion at the ductular level. This stimulation may occur indirectly *via* CCK release or *via* a direct mechanism, but does not occur *via* duodenal acidification. Bombesin also decreases cholesterol output, perhaps *via* physiologic increases in glucagon. The observed choleretic effects of bombesin occur in a dose-dependent manner, but a physiologic role for bombesin in hepatic bile formation has not been proven.

Acknowledgment

We wish to thank Mary P. Scott for her expert secretarial assistance.

References

1. Anastasi A, Erspamer V, Bucci M. Isolation and structure of bombesin and alytesin, two analogous active peptides from the skin of the European amphibians Bombina and Alytes. Experientia 1971; 27:166–167.
2. Bertacceni G, Erspamer V, Melchiorri P, et al. Gastrin release by bombesin in the dog. Br J Pharmacol 1974; 52:219–225.
3. Fender HR, Curtis PJ, Rayford PL, et al. Effect of bombesin on gastrin and secretin and on gastric and pancreatic secretion. Physiologist 1975; 18:212.
4. Duval JW, Saffouri B, Weir GC, et al. Stimulation of gastrin and somatostatin secretion from the isolated rat stomach by bombesin. Am J Physiol 1981; 241:G242–247.
5. Fender HR, Curtis PJ, Rayford PL, et al. Effect of bombesin on serum gastrin and cholecystokinin in dogs. Surg Forum 1976; 27:414–416.
6. Erspamer V, Improsta G, Melchiorri P, et al. Evidence of cholecystokinin release by bombesin in the dog. Br J Pharmacol 1974; 52:227–232.
7. Iwatsaki N, Petersen OH. In vitro action of bombesin on amylase secretion, membrane potential, and membrane resistance in rat and mouse pancreatic acinar cells. J Clin Invest 1978; 61:1635–1644.
8. McDonald TJ, Ghatei MA, Bloom SR, et al. A qualitative comparison of canine plasma gastroenteropancreatic hormone response to bombesin and porcine gastrin-releasing peptide. Regul Pept 1981; 2:293–304.
9. Schusdziara V, Rouiller D, Harris V, et al. Effect of bombesin upon plasma somatostatin-like immunoreactivity, insulin, and glucagon in normal and chemically sympathectomized dogs. Regul Pept 1980; 1:89–96.
10. Pontirrvli AE, Alberetto M, Restelli L, et al. Effect of bombesin and ceruletide on prolactin, growth hormone, lutenizing hormone, and parathyroid hormone release in normal human males. J Clin Endocrinol Metab 1980; 51:1303–1305.
11. Portras P, Tasse D, Laprise P. Stimulation of motilin release by bombesin in dogs. Am J Physiol 1983; 245:G249–256.
12. Rokaens A, McDonald TJ. Release of neurotensin-like immunoreactivity from rat intestine following administration of bombesin. Acta Physiol Scand 1980; 110:326.
13. Bloom SR, Ghatei MA, Christofides ND, et al. Release of neurotensin, enteroglucagon, motilin, and pancreatic polypeptide by bombesin in man. Gut 1979; 20:A912–913.
14. McDonald TJ, Jornvall H, Nilsson G, et al. Characterization of a gastrin releasing peptide from porcine non-antral gastric tissue. Biochem Biophys Res Commun 1979; 90:227–233.
15. Bloom SR, Ghatei MA, Wharton JW, et al. Distribution of bombesin in human alimentary tract. Gastroenterology 1979; 76:1103.
16. Reeve JR, Walsh JH, Chew P, et al. Amino acid sequences of three bombesin-like peptides from canine intestine extract. J Biol Chem 1983; 258:5582–5588.
17. Kaminski DL, Deshpande YG. Effect of somatostatin and bombesin

on secretin-stimulated ductular bile flow in dogs. Gastroenterology 1983; 85:1239–1247.
18. Jones RS, Yee TK, Michelsen GE. A modified cannula for gastric and intestinal fistulae. J Appl Physiol 1971; 30:427–428.
19. Talalay P. Enzymic analysis of steroid hormones. In *Methods of Biochemical Analysis,* Vol. 8. New York: John Wiley and Sons, 1960; 119.
20. Abell LL, Levy BB, Brodie BB. A simple method for the estimation of total cholesterol. J Biol Chem 1952; 195:357.
21. Fiske LH, Subbarow Y. The colorimetric determination of phosphorus. J Biol Chem 1925; 66:375.
22. Forker EL. Two sites of bile formation as determined by mannitol and erythritol clearance in the guinea pig. J Clin Invest 1967; 46: 1189–1195.
23. Jones RS, Grossman MI. Dose response relationship of the choleretic effect of histamine. Am J Physiol 1969; 216:335–339.
24. Wheeler HO, Mancusi-Ungaro PL. Role of bile ducts during secretin choleresis in dogs. Am J Physiol 1966; 210:1153–1159.
25. Nahrwold DL. Secretion by the common duct in response to secretin. Surg Forum 1971; 22:386–387.
26. Barnhardt JL, Combes B. Erythritol and mannitol clearances with taurocholate and secretin induced choleresis. Am J Physiol 1978; 234:E146–E156.
27. Russel TM, Searles GL, Jones RS. The choleretic mechanism of sodium taurocholate, secretin and glucagon. Surgery 1975; 77: 498–504.
28. Miyata M, Rayford PL, Thompson JC. Hormonal (gastrin, secretin, and cholecystokinin) and secretory effects of bombesin and duodenal acidification in dogs. Surgery 1980; 87:209–215.
29. Schirmer BD, Kortz WJ, Miller RJ, et al. Glucagon lowers canine biliary cholesterol output at physiologic doses. Dig Dis Sci (in press).
30. Matsuyama T, Namba M, Nomku K, et al. Decrease in blood glucose and release of gut glucagon-like immunoreactive materials by bombesin infusion in the dog. Endocrinol Jpn 1980; 27:115–119.
31. Vaysee N, Pradayrol L, Chayvialle JA, et al. Effects of somatostatin-14 and somatostatin-28 on bombesin-stimulated release of gastrin, insulin, and glucagon in the dog. Endocrinology 1981; 108:1843–1847.
32. Varner AA, Modlin IM, Walsh JH. High potency of bombesin for stimulation of human gastrin release and gastric acid secretion. Regul Pept 1981; 1:289–296.
33. Erspamer V, Melchiorri P. Amphibian skin polypeptides active on the gut. J Endocrinol 1976; 70:12P–13P.
34. Polak JM, Bloom SR, Solcia E, et al. Distribution of a bombesin-like peptide in human gastrointestinal tract. Lancet 1976; 1:1109–1110.
35. Buffa R, Solovieva I, Fiocca R. Localization of bombesin and GRP (gastrin releasing peptide) sequences in gut nerves or endocrine cells. Histochemistry 1982; 76:457–467.