

## The Choloretic Response to Feeding in Dogs (34293)

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Fritz and Brooks (1) demonstrated the potent choloretic effect of feeding in dogs. The present study was done to determine the relation between the amount of food eaten and the amount and composition of the bile secreted.

**Methods.** Four mongrel dogs, weighing 16–23 kg, were prepared by cholecystectomy, ligation of the lesser pancreatic duct, insertion of a Thomas cannula (2) into the duodenum opposite the opening of the common bile duct, and insertion of a Thomas cannula into the stomach. Starting at least 2 weeks after surgery, experiments were performed no oftener than 3 times weekly. Following an 18-hr fast, the gastric and duodenal cannulas were opened, and a polyethylene tube (Intramedic PE 190, outside diameter 1.7 mm) was inserted 5–6 cm into the common bile duct and brought out through a small hole in a cork used to occlude the duodenal fistula. The gastric fistulas were closed after the stomachs were found to be empty. Bile was collected at 15-min intervals for the duration of the experiment.

Throughout each experiment the dogs received a continuous intravenous infusion from a peristaltic pump (Harvard Apparatus Co., Dover, Mass.) at a rate of 64 ml/hr. All dogs received 0.15 M NaCl during the first four 15-min periods, then 0.5% sodium taurocholate (Maybridge Chemical Co., Ltd., Tintagel, N. Cornwall, U.K.) was added to the infusion and continued for the duration of the experiment. After sodium taurocholate had been infused for four 15-min periods, the dogs were fed either 1.25, 2.5, 5, 10, 20, 40, or 80 g/kg of canned Friskies dog food. Two experiments were done with each quantity of

food on each of the four dogs. The dogs ate all test meals vigorously. Control experiments were done without feeding. Bile samples were collected at 15-min intervals for 4 hr following feeding.

Other feeding experiments were performed by feeding 10 g/kg of dog food every 15 min during the feeding period until the dog would eat no more. Bile volumes were recorded. Bicarbonate concentrations were determined by adding 0.5 ml of bile to 1.0 ml of 0.1 N HCl, boiling, cooling, and back-titrating to pH 7.0 with 0.2 N NaOH using an automatic titrator and pH meter (Auto-burette, Radiometer, Copenhagen). Chloride concentration was estimated with a chloridometer (Buchler-Cotlove, N.J.). Bile salt concentration was calculated by the method of Wheeler and Ramos (3). Dose-response lines were evaluated with tests of dependence and linearity (4). Bile salt outputs were evaluated by analysis of variance while comparisons of multiple feeding experiments were made with the *t* test for paired values (4). As used in the text "significant" means  $p < 0.05$ .

**Results. Bile volume** (Fig. 1). All doses of food produced increases in bile flow. The highest mean peak bile flow, 5.3 ml/15 min, and the highest total bile volume, 66.0 ml/4 hr, occurred in response to the largest feeding

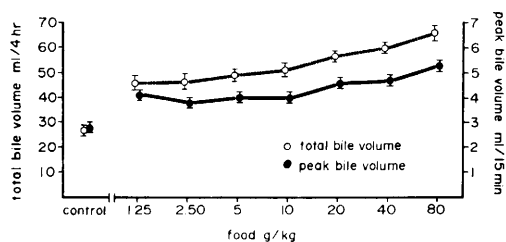


FIG. 1. Bile volume response after feeding; in Figs. 1–4 vertical lines indicate SEM.

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(80 g/kg). Analysis of variance showed that peak bile flow was significantly higher than control for all levels of feeding, however the peak responses to 1.25, 2.5, 5.0, and 10.0 g/kg of food did not differ significantly.

**Bicarbonate output** (Fig. 2). All doses of food increased bile bicarbonate output. The highest mean peak bicarbonate outputs, 270.3  $\mu\text{Eq}/15\text{ min}$ , and the highest mean 4-hr bile bicarbonate outputs, 3351.8  $\mu\text{Eq}/4\text{ hr}$ , occurred after 80 g/kg of food.

**Bile salt output** (Fig. 3). There was no significant increase in total 4-hr or peak 15-min bile salt output after feeding.

**Dose-response relationships.** Dose-response lines were drawn relating the peak bile volume and bicarbonate output as well as the 4-hr bile volume and bicarbonate output to the logarithm of food doses 5, 20, and 80 g/kg. The bile volumes and bicarbonate outputs were linearly related to and dependent

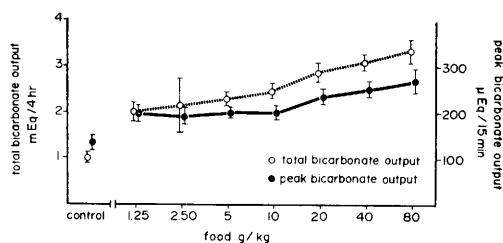


FIG. 2. Bile bicarbonate output after feeding.

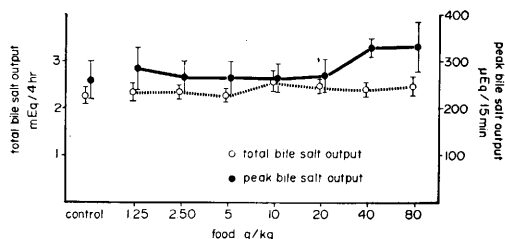


FIG. 3. Calculated bile salt output after feeding.

upon the logarithm of the food dose (Fig. 4).

**Relationship of bile flow rate to bicarbonate concentration.** Bile flow rate was plotted against bicarbonate concentration for the four consecutive 15-min periods after feeding (Fig. 5). The linear regression was

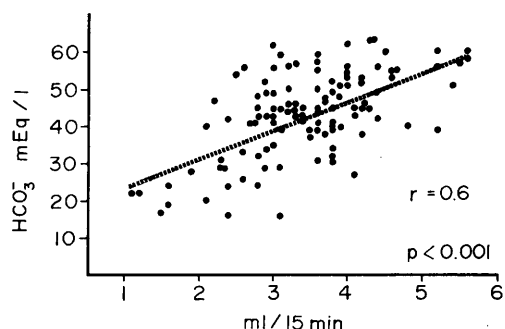


FIG. 5. Relationship between bile bicarbonate concentration and bile flow during feeding choleresis; the line for these data is represented by the equation  $Y = 17.3 + 7.5X$ .

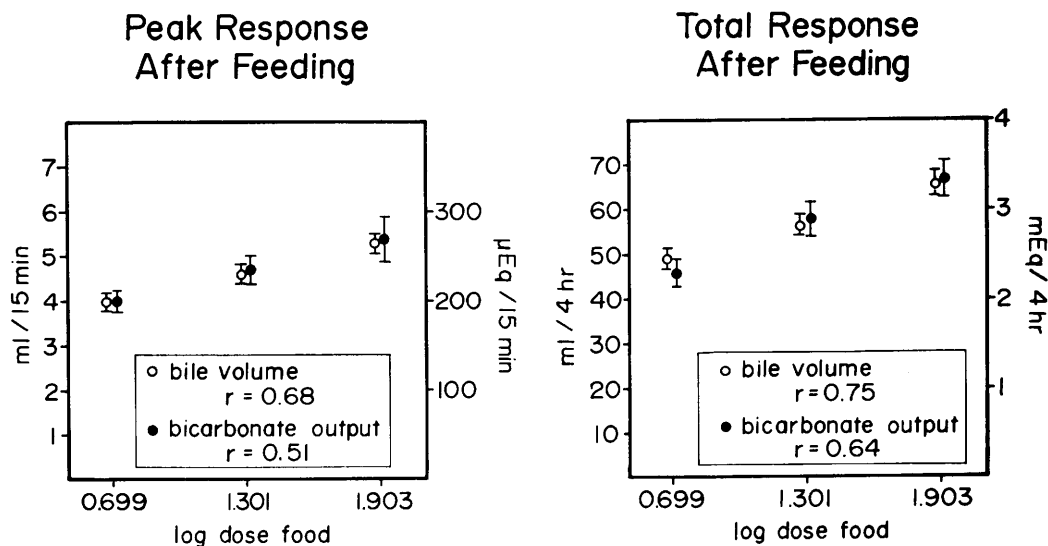


FIG. 4. Feeding choleresis dose-response relationships.

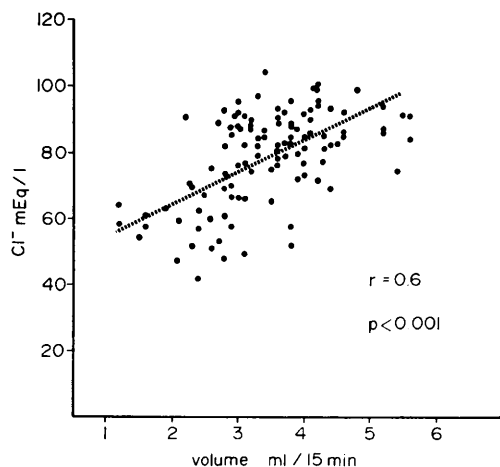


FIG. 6. Relationship between bile chloride concentration and bile flow during feeding choleresis; the line for these data is represented by the equation  $Y = 49.5 + 8.5X$ .

calculated and bicarbonate concentration was dependent upon bile flow.

*Relationship of bile flow rate to chloride concentration.* Bile flow rate was plotted against chloride concentration for the four consecutive 15-min periods after feeding (Fig. 6). The linear regression was calculated and chloride concentration was dependent upon bile flow.

*"Electrolyte fraction" of bile after feeding* (Fig. 7). Using the equation of Wheeler and

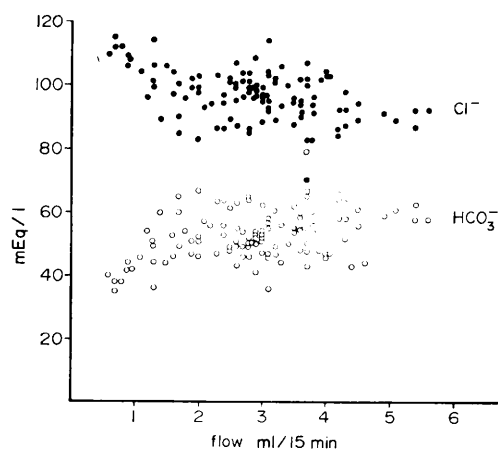


FIG. 7. The relationship between the volume, bicarbonate concentration, and chloride concentration of the "electrolyte fraction" of bile during feeding choleresis.

Ramos (3) the volume, bicarbonate concentration, and chloride concentration of the "electrolyte fraction" of the bile obtained during the first four 15-min periods after feeding was calculated. There was a tendency for chloride concentration to decrease and for bicarbonate concentration to increase as the volume of the electrolyte fraction increased. The concentrations of both of these ions appeared to plateau at volumes of about 2.0 ml/15 min and further increase in the volume of the "electrolyte fraction" resulted in no further change in its chloride or bicarbonate concentration.

*Multiple feeding.* When dogs were fed 10 g/kg of food every 15 min, the amount of food eaten ranged from 6 to 12 portions. The peak 15-min response after feeding multiple meals was compared with peak response after single feeds of 40 g/kg. The bile secretory response during the first hour following a meal of 40 g/kg was also compared with choleresis elicited by the initial 4 consecutive quarter hourly meals of 10 g/kg. Table I compares the peak 15-min and 1-hr bile volumes and bicarbonate outputs for multiple feeding of 10 g/kg and single feeding of 40 g/kg. There were no significant differences between the responses after single and multiple feeds.

*Discussion.* The data from this experiment show that feeding choleresis is dependent upon the quantity of food eaten. This observation is comparable to that of Thomas and Forrest (5) who noted a quantitative relationship between acid output from Heidenhain pouches in dogs and the amount of meat fed. Regarding choleresis, however, multiple meals failed to produce higher biliary flows than the same amount of food as a single feeding. Thomas and Forrest (5) found that in the case of gastric secretion multiple feeding produced larger responses.

Peak bile volume did not vary significantly with feeds ranging from 1.25 to 10 g/kg, but with feeds between 10 and 80 g/kg there was a linear relation between size of feed and peak bile volume (Fig. 1). We can offer no explanation for this observation. The peak bile volume occurred in the third to seventh 15-min period after feeding and the time of

TABLE I. Comparison of Bile Flow and Bicarbonate Output with Multiple and Single Meals.

	Peak vol (ml/15 min ± SEM)	Peak HCO <sub>3</sub> out- put (μeq/15 min ± SEM)	First hr vol (ml/hr ± SEM)	First hr HCO <sub>3</sub> output (μeq/hr ± SEM)
Re-feed 10 g/kg	5.1 ± 0.3	270.2 ± 24.9	15.1 ± 0.5	684.0 ± 47.2
Feed 40 g/kg	4.7 ± 0.2	252.8 ± 17.7	15.9 ± 0.5	730.7 ± 42.1

occurrence of peak was not related to size of feed.

The increments of bicarbonate and chloride concentrations with increasing bile flow after feeding are similar to the observations of Wheeler and Ramos (3) made during secretin choleresis. We have seen a similar linear relationship between bile flow rate and bicarbonate and chloride concentrations during secretin choleresis in dogs (unpublished observations). Also, the composition of the "electrolyte fraction" with varying flow rates during feeding choleresis is similar to that shown by Wheeler and Ramos (3) during secretin choleresis.

Nahrwold and Grossman (6) demonstrated that bile in the intestine was an important factor in the choleresis after feeding, but feeding during interruption of the enterohepatic circulation produced a secretin-like choleresis. In addition to the enterohepatic circulation of bile salts, gastrin (7), cholecystokinin-pancreozymin (8), and vagal stimulation (1) probably contribute to feeding choleresis.

*Summary.* Mongrel dogs were prepared by cholecystectomy, ligation of the lesser pancreatic duct, and insertion of a Thomas cannula into the duodenum opposite the opening of the common bile duct. The common bile duct was cannulated through the duodenal cannula and bile flow and composition were observed after feeding graded quantities of canned dog food. The magnitude of the choleresis was dependent upon and linearly

related to the logarithm of the quantity of food eaten. Multiple feeds did not produce greater peak 15-min bile flow or hourly bile flow than a single feed of an equal amount of food. After feeding bicarbonate and chloride, concentration in bile increased as bile flow increased. The relationships between volume, chloride concentration, and bicarbonate concentration of the calculated "electrolyte fraction" during feeding choleresis were similar to those seen during secretin choleresis.

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