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Experimental Study of Bile Duct Reconstruction by Jejunal Interposition and by Roux-Y Jejunal Limb

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ABSTRACT : In studies to elucidate the mechanism of gastric acid hypersecretion after Roux-Y bille diversion, Heidenhain pouches were constructed in 19 healthy mongrel dogs. The construction of 40-cm blind ended Roux-Y jejunal limbs in 5 dogs caused significant increase in total 24-hour acid secretion, an average rise of 148 percent of the control levels. This increase was further augmented when bile flow was directed into the jejunum via these limbs. Similar significant acid increase occurred when the end of a 40-cm blind jejunal segment was anastomosed to the side of the duodenum in 6 dogs. Complete diversion of bile into the duodenum via the jejunal segment produced even greater acid output, an average of a 138 percent increase, although this was reversed to normal by shortening the jejunal segment. Primary construction of jejunal interpostiion choledochoduodenostomy in 4 dogs or choledochojejunostomy Roux-en-Y in 4 dogs also induced hypersecretion. Serum gastrin levels were not changed significantly throughout this study except when a 40-cm blind ended jejunal segment was inserted into the duodenum. Results of liver function tests remained unchanged.

INTRODUCTION

Bile diversion, gastric hypersecretion, Roux-Y choledochojejunostomy, jejunal interpostion choledochoduodenostomy, blind ended Roux-Y jejunal limb, blind ended jejunal segment.

Complete exclusion of bile from the duodenum has been well demonstrated to increase gastric acid secretion and form peptic ulcers in experimental animals. Menguy[1] and Breen *et al*[2] reported that a statistically significant increase of gastric acid secretion occurred after Roux-Y choledochojejunostomy, although subsequent authors[2] observed no significant rise in dogs with choledochoduodenostmy or choledochocholedochostmy. In a clinical study, Nielsen and associates[3] found increased gastric acid following bile diversion via a Roux-Y jejunal limb, and also showed that serum gastrin and gastrin in the antral mucosa coincidentally increased. Others have reported clinical complications subsequent to bile diversion. McArthur and Longmire[4] noted the occurrence of peptic ulcer diseare after choledochojejunostomy in 12 percent of patients with benign extrahepatic biliary obstruction, but other sizable series have been reported without ulcer formation.

It has been proposed that gastric hypersecretion following experimental bile diversion results from fatty degeneration of the liver or lack of adequate gastric inhibitory duodenal hormone in experimental models. Altered biosynthesis and release of gastrin have been suspected in clinical studies.

The major differences of anatomical and physiological disarrangement between Roux-Y choledochojejunostomy and choledochoduodenostmy are not only whether bile flows into

the duodenum or into the jejunum but also whether a defunctionalized jejunal segment is interposed between the biliary duct system and the intestinal tract. The important relationship that may exist between the jejunal segment and hypersecretion has received little attention in the literature.

The present study was designed to determine whether an isolated jejunal segment might play an important role in the genesis of the hypersecretion subsequent to bile diversion. For this purpose, an isolated blind jejunal segment was prepared and then anastomosed to the duodenum. Denervated pouch acid secretion before and after bile diversion through this segment was compared to acid secretion before and after bile diversion through a Roux-Y jejunal limb into the duodenum.

METHODS

This experiment involved 19 adult mongrel dogs of both sexes weighing 20 to 28 kilograms. All of the operations were preformed aseptically under sodium pentobarbital anesthesia. A denervated pouch of stomach (Heidemhain pouch) was constructed in each animal and drained by a Gregory cannula. To effect complete denervation, all connective tissue and nerves from the splenic vein and artery were stripped for a distance of several centimenters. After a recovery period of 4 to 5 weeks, the integrity of vagal denervation to the pouch was assessed by an insulin hypoglycemia test using 0.5 unit per kilogram intramuscularly and analyzing gastric secretion from the pouches every 15 minutes over the ensuing 2 hours. The secretory response of the pouch was also determined during the 2 hours after the intramuscular injection of 1.0 mg histalog per kilogram in the fasting state. In each pouch, complete denervation and reliable responce to stimulation by histalog were confirmed. Quantitative 24-hour gastric secretion from the pouch was then collected for at least 30 days while the dogs were maintained on a standard diet of pelleted dry mael with water ad libitum. These collections served as a control.

The concentration of total acid (free + combined acid) was determined by titration of an aliquot sample with 0.1 N sodium hydroxide to a-pH of 8 to 10 using Topfer's reagent as an indicator. The results were expressed as milliequivalents per liter. From the volume collectedm, total acid output per unit time was calculated, them expressed as milliequivalents per hour for fractional studies and per 24 hours for daily collections. After a period of control collections, the dogs were divided into 4 groups and subjected to further operations. Student paired t-test was used to evaluate the significance of the changes in gastric secretion. Throughout this study p value of 0.05 was taken as being significant.

Group I (6 dogs): In the first stage, an isolated segment of the jejunum, 40 cm in length, was prepard approximately 15 cm distal to the ligament of Treitz nad placed in a retrocolic postion. The proximal end of the isolated segment was closed in two layers and sutured to the lateral abdominal wall to prevent intussusception of the segment and for ready identification at subsequent operations. The distal end of the segment was then anastomosed to the side of the second portion of the duodenum near the level of the entrance to the common bile duct, approximately 7 cm from the pylorous. Jejunal continuity was restored by an end-to-end jejunojejunostomy (**Fig. 1-a**). In the second stage, the common bile duct was isolated and divided close to the lateral margin of the duodenum. The distal stump was ligated and the proximal duct was anastomosed to the isolated jejunal segment as shown in **Figure 1-b.** This anastomosis was performed using a modified Coffey's technique[5] with a silicon tube splint of 0.2 to 0.3 cm diameter. In the second stage, a partial resection of the middle portion of the interposed jejunal segment was performed on 4 dogs to reduce the length to less than 15 cm. Continuity of the interposed jejunum was then reestablished by an end-to-end anastomosis with interrupted sutures in two layers (**Fig. 1-c**). The remaining 2 dogs died from unrelated complications and were excluded from this final stage operation.

Group II (5 dogs): In the first stage, the jejunum was divided at the site of the first major vascular arcade, approximately 15 cm distal to the ligament of Treitz. The distal end of the

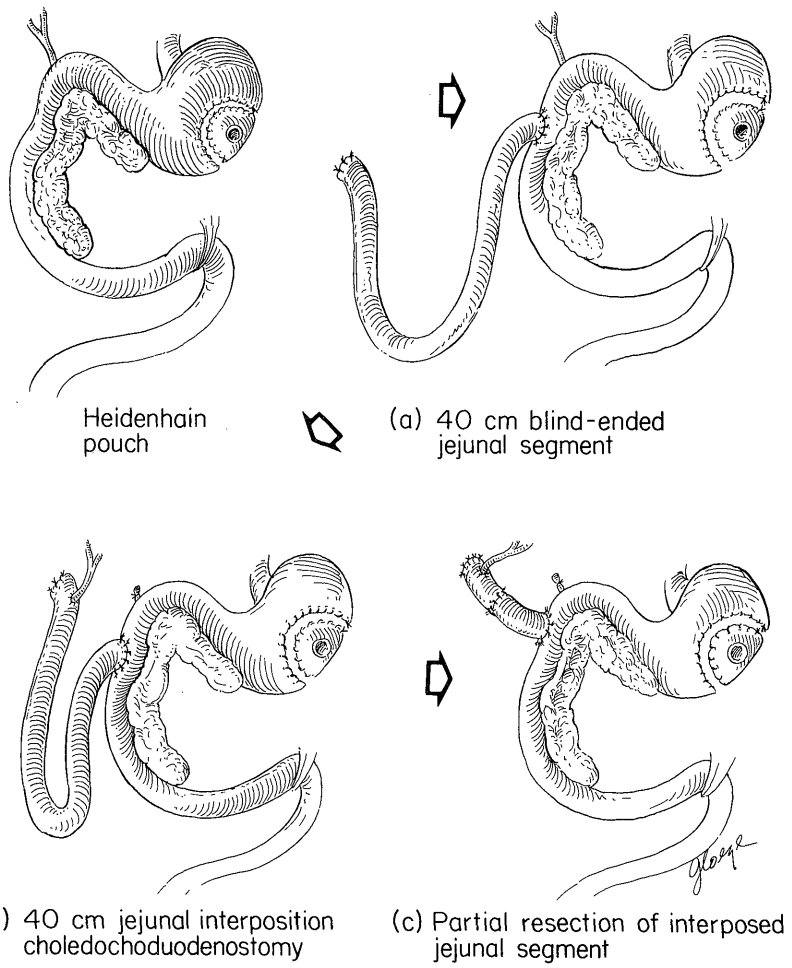

Fig. 1. Experimental Model: jejunal interposition choledochoduodenostomy.

jejunum was closed in two layers and fixed to the lateral abdominal wall through the retrocolic spase. The proximal end of the jejunum was anastomosed end-to-side to the jejunum, 40-cm distal to the site of the primary diversion, thereby creating a blind-end Roux-jejunal limb 40 cm in length (**Fig. 2-a**). In the second stage, complete bile diversion into the jejunum via this limb was established by implantation of the common bile duct into the proximal portion of the Roux-Y jejunal limb as in group I (**Fig. 2-b, c**).

Group III (4 dogs): A primary 40-cm jejunal interposition choledochoduodenostomy was constructed after the control period. The 40-cm interposed segment was prepared in the same manner as applied in group I.

Group IV (4 dogs): A primary 40-cm Roux-Y choledochojejunostomy was constructed. The 40-cm Roux-jejunal limb was prepared in the same fashion as described for group II.

After an additional 4 to 5 weeks of recovery following each operation, the histalog test was repeated on each dog to reevaluate the validity of the secretion from the pouch. The 24-hour gastric juice collection was conducted for at least 30 days and analyzed as before.

Samples of peripheral venous blood of the dogs in group I and II were used for measurment of serum gastrin levels by a specific radio-

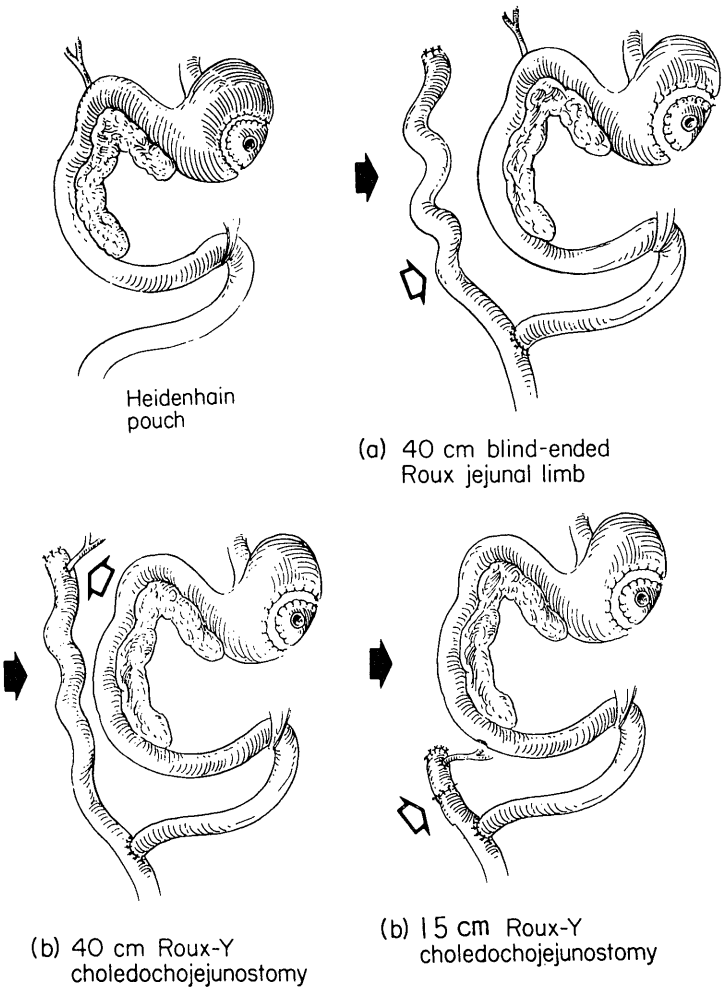

Fig. 2. Experimental Model: choledochojejunostomy Roux-en-Y.

immunoassy in the fasting state and in 1-hour samples for 6 hours after a test meat meal.

RESULTS

Group I: The results of daily analysis of the volume, total acid concentration and total acid output are presented in **Tables I, II,** and **III,** respectively. The volume from the pouch of each dog following construction of 40-cm blind-ended jejunal segments anastomosed to the duodenum increased significantly from a mean control level of 301 m*l*/24 hours to a mean level of 572 m*l*/24 hours (120 percent). These increases were further raised with statistical significance in 4 of the 6 dogs after subsequent complete bile diversion into the duodenum via these segments. By shortening the interposed jejunal segments to less than 15 cm, the higher volumes were depressed to somewhat lower levels than those found in the control period. Variations of total acid concentrations throughout this study in this group were less than 15 percent above or 24 percent below the control levels. There was no correlation between these relatively small changes in total acid concentration and operattive procedure. The mean total acid output in this group was 46 mEq/24 hours in the control period. This value was raised to a level of 89 mEq/24 hours after con-

Table 1. Total Acid Output (mEq/24 hr) from Heidenhain Pouch in Group I

Dcg #	Control Period (a) Heidenhain Pouch only	2nd Operation (b) 40cm Blind Ended Jejunal Segment to Duodenum	3rd Operation (c) JICD@ 40cm Jejunal Interposed	4th Operation (d) JICD@ 15cm Jejunal Interposed	Per Cent Increase in Total Acid Output $\frac{b-a}{a}\times 100$,	$\frac{c-a}{a}\times 100$,	$\frac{d-a}{a}\times 100$,
1	43±11	103±36*	137±53	—	139	218	
2	25±10	97±22*	123±18+	—	288	392	
3	24±10	89±20*	42±22	38±13	270	75	58
4	104±33	148±38*	177±39+	98±23	42	70	− 6
5	41±16	56±25*	95±35+	27±14	36	131	−35
6	37±14	43±11*	38± 9	27± 9	14	3	−27
mean					131	147	− 2

* ; $p<0.05$ vs Control group @ ; Jejunal Interpostion Choledochoduodenostomy
\+ ; $p<0.05$ vs 2nd operation period

Table 2. Total Acid Output (mEq/24 hr) from Heidenhain Pouch in Group II

Dcg #	Control Period (a) Heidenhain Pouch only	2nd Operation (b) 40cm Blind Ended Roux-Y Jejunal Limb	3rd Operation (c) 40cm Roux-Y Choledoch-Jejunostomy	4th Operation (d) 15cm Roux-Y Choledoch-Jejunostomy	Per Cent Increase in Total Acid Output $\frac{b-a}{a}\times 100$,	$\frac{c-a}{a}\times 100$,	$\frac{d-a}{a}\times 100$,
7	58±24	96±32*	111± 4+	72±12	66	91	24
8	29±12	73±13*	100±33+	36±14	151	244	24
9	66±20	93±28*	117±39	45± 9	41	77	−31
10	8± 3	13± 4*	21± 5+	—	62	162	—
11	18±10	115±22*	117±16	55±18	538	550	205
mean					171	225	55

* ; $p<0.05$ vs Control group
\+ ; $p<0.05$ vs Control and 2nd operation period

structing 40-cm blind ended jejunal segments, an increas of 131 percnet; further increase of a mean level of 102 mEq/24 hours occurred after bile diversion to the duodenum through these segments (147 percent). When compared with the levels before and after bile diversion, 3 of the 6 dogs had statistically significant increases after bile diversion, wherease after partial resection of the interposed segments, these higher values diminished to a mean level of 48 mEq/24 hours, almost the same as the mean value of the control periods in the same dogs. (**Table 1**)

Group II: The volume of the control period in this group was 224 ml/24 hours. This value rose to a level of 498 m*l*/24 hours after construction of 40-cm blind ended Roux-jejunal limbs and to a level of 642 m*l*/24 hours when bile was routed into the jejunum. Compared to the control values, significant increase were observed in all of the 5 dogs with blind Roux-jejunal limbs and after bile diversion. Compared before and after bile diversion, a significant increase occurred in 4 dogs after diversion. Total acid concentrartion in this group varied considerably within 20 percent above or 14 percent below the levels of the control periods and was not significantly affected by the operative procedures. The mean total acid output increased markedly from a control level of 36 mEq/24 hours to 78 mEq/24 hours during the period of the blind Roux-jejunal limb, with a further rise of 93 mEq/24 hours during the period of complete bile diversion into the jejunum, an increase of 171 and 225 percent, respectively. (**Table 2**)

Group III: Primary construction of 40-cm jejunal interposition choledochoduodenostmy

Table 3. Total Acid Output (mEq/24 hr) from Heidenhain Pouch in Group III and IV

Dog #	Group III Acid Output (mEq/24 hr)			Dog #	Group IV Acid Output (mEq/24 hr)		
	Control Period	40cm JICD	Per Cent Increase		Control Period	40cm CJ* Roux-Y	Per Cent Increase
12	97±23	63±22	−6	16	55±30	70±28	27
13	42±22	84±36*	100	17	36±18	48±32	33
14	38±11	56±39	47	18	104±49	104±49*	316
15	25±16	54±17*	116	19	69±23	69±23*	57
mean			64	mean			108

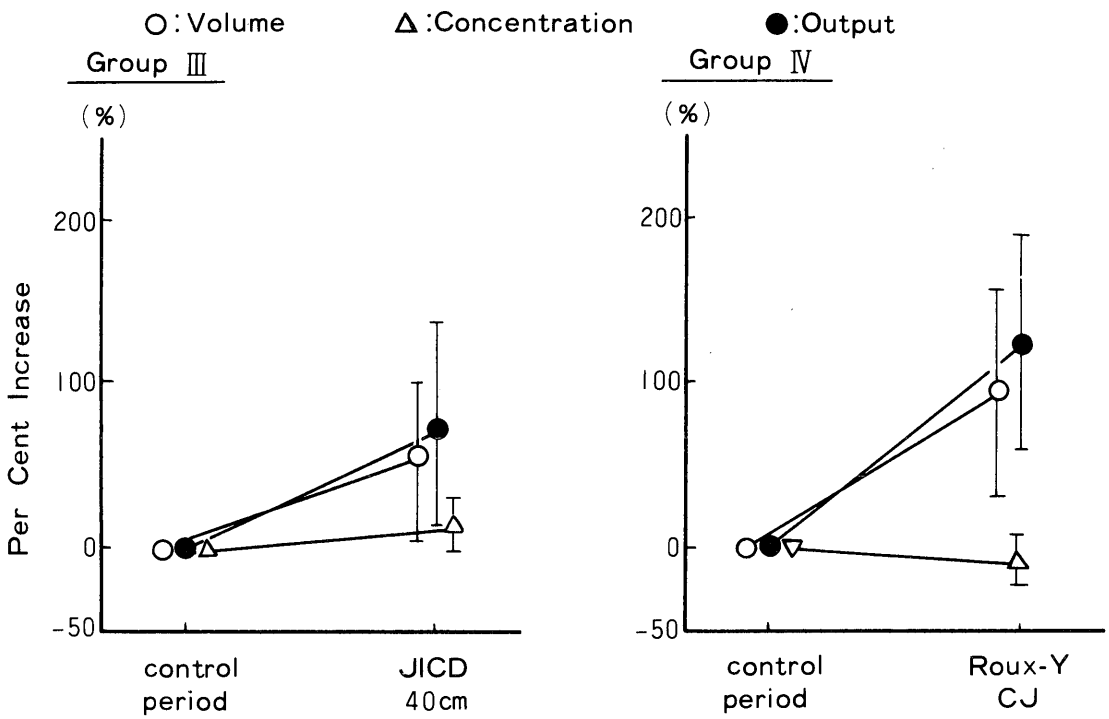

Fig. 3. Comparison of mean per cent of control changes of gastric secretion of groups III-IV. Vertical lines represent SD. Both groups show a increase, but not significant ($P>0.05$).

caused augmentation of the volume, total acid concentration, total acid output from a control level of 290 m*l*/24 hours, 138 mEq/*l* and 43 mEq/24 hours to 411 m*l*/24 hours, 140 mEq/*l* and 64 mEq/24 hours, respectively ; 2 of the 4 dogs had significant elevation of volume, concentration and acid output, but one dog shiwed a statistically insignificant decrease in volume. concentration and acid output.

Group IV : All of the 4 dogs had significant increases in volume, and 3 also had significant increase in total acid output. However, total acid concentration was not changed significantly except for one dog, which rose 30% above the control level and also produced a total acid output more than 3 times the control (**Table 3. Fig. 3**).

Autopsy of experimental animals of Group I, II, III, IV was performed after histamine stimulation 30mg/day/40day. No ulcer formation was noticed in 5 dogs of bile diversion into the duodenum, although 50% incidence of duodenal

Table 4. Incidence of Ulcer Formation

Group I Peptic Ulceration following Jejunal Interposition Choledochoduodenostomy

dog #	duration (day)	stomach		duodenum		jejunum		gastric secretion*
		ulcer	erosion	ulcer	erosion	ulcer	erosion	
1.	240	–	–	–	–	–	–	70%
2.	122	–	–	–	–	–	–	220
3.	92	–	–	–	–	–	–	73
4.	93	–	–	–	–	–	–	320
5.	90	–	–	–	10×10mm	–	–	119
	127	0/5	0/5	0/5	1/5	0/5	0/5	164

Group II Peptic ulceration following Roux-Y choledochojejunostomy

6.	131	–	–	–	10×10mm	–	8×8	125
7.	124	–	–	10× 8	10×8	–	5×8	445
8.	140	–	–	15×15 20×20 20×15	diffuse	–	diffuse	151
9.	133	–	–	–	20×15	–	diffuse	151
	132	0/4	0/4	2/4	4/4	0/4	4/4	218

* : Per cent increase

Table 5. Incidence of Ulcer Formation

Group III Peptic Ulceration following primary Interposition Choledochoduodenostomy with Histamine Stimulation (30mg/day/40days)

dog #	duration (day)	stomach		duodenum		jejunum		gastric secretion*
		ulcer	erosion	ulcer	erosion	ulcer	erosion	
10	320	–	multiple	–	5×4, 4×3	–	–	125%
11	98	–	–	–	–	–	–	50
12	88	–	multiple	–	15×7, 5×5	–	–	178
	168	0/3	2/3	0/3	2/3	0/3	0/3	117

Group IV Peptic Ulceration following primary Choledochojejunostomy with Histamine Stimulation (30mg/day/40days)

13	65	multiple	multiple	–	15×15	–	–	165
14	109	–	–	7× 7	–	7× 7	–	/
15	106	–	–	15×10 10× 5 10× 6 10× 8	2×5 4×6	20×18	–	/
	93	1/3	1/3	2/3	2/3	2/3	0/3	165

ulcer formation was revealed in the dogs with bile diversion into the jejunum. Erosion of the duodenum and jejunum was seen in all the dogs with Roux-Y jejunum limb but not seen in the dogs with inter-position choledochojejunostomy (**Table 4, 5**).

DISCUSSION

The present study confirmed the results previously reported by Forrest and Longmire[6], who demonstrated that disconnecting a segment of small bowel from the mainsteam flow of intestinal contents significantly increased

gastric acid secretion, and in addition, showed that complete bile diversion through the segment (whether into the duodenum or into the proximal portion of the jejunum) further elevated the established gastric hypersecretion. However, an impressive decrease of the augmented hypersecretion is achieved by shortening the interposed jejunal segment to less than 15 cm in length.

Hyperacidity after prolonged complete bile diversion by choledochojejunostomy Roux-en-Y has been well documented in experimental animals.[1,2] The mechanism responsible for the hypersecretion after this procedure is still largely unknown. In 1962, using bile diversion by a Roux-en-Y jejunal loop to the terminal ileum, Menguy[1] produced hypersecretion of gastric acid in 4 of the 5 dogs. From the findings of delayed onset of hypersecretion, coincidental liver disease and failure of gastric function to return to normal levels after restoration of biliary secretion to the duodenum in 2 dogs with irreversible liver damage, they suggested that gastric hypersecretion occurring after biliary diversion was related to liver disease (fatty liver) and diminished ability of the liver to destroy histamine absorbed from the intestine. This proposal was supported by Silen,[7] who found that gastric hypersecretion induced by ligation of the common bile duct in dogs failed to be reversed to the control levels by choledocho-duodenostmy, if the liver damege was irreversible. In 1963, Breen *et al*[2] reported that a statistically significant rise of gastric acid secretion after choledochojejunostomy Roux-en-Y occurred in 4 or 5 dogs, whereas no significant increase was observed in 6 dogs after choledocho-duodenostomy or choledochocholedochostomy. They explained their results by proposing that impairment of the duodenal mechanism responsible for inhibiting gastric secretion was involved.

These previous authors have related the gastric acid hypersecretion to the site of bile diversion. Although bile in the intestine has been demonstrated to play an important role in the gastric inhibitory mechanism through absorption of fatty acid, inhibition of gastric acid secretion by fat can be elicited from the entire intestine as proved by Konturek and Groussman.[8] In Roux-en-Y choledocho-jejunostomy, bile flows into the proximal jejunum, and thus this inhibitory mechanism may take place normally.

Prolonged bile diversion may be followed by some complications such as malnutrition or impaired liver function that may alter gastric secretion.[1] To avoid this complication, Nahrwold and Grossman[9] studied the short term effect of complete bile exclusion from the intestine in dogs with denervated gastric pouches. When food was given[3] hours after initiating bile exclusion by common bile duct cannulation, the gastric secretory response was markedly depressed, whereas no depression occurred when food was given 1 hour after cannulation. In the present stydy, bile flow into the duodenum through an interposed jejunal segment resulted in similar quantities of hypersecretion to that observed after bile diversion through a Roux-jejunal limb into the jejunum. In view of these findings, it seems likely that the mechanism producing hyper-secretion after bile diversion, particularly by a Roux-en-Y choledochojejunostomy, is not attributable to impairment of the duodenal mechanism responsible for inhibiting gastric secretion.

The fact that mere construction of a 40-cm blind-end defunctionalizad jejunal segment produced a constant and fairly marked increase of acid secretion and that blind jejunal segment-induced hypersecretion was further augmented by bile diversion through the segment (whether into the duodenum or into the jejunum) strongly suggest that the mucosa of the isolated jejunal segment itself is involved in the reaction. In other words, the segment itself may be capable of releasing an acid stimulant. Similar convincing evidence that the isolated intestinal segment facilitates the intestinal phase of gastric secretion is seen in the study of Kerr and Elliott.[10] They showed that construction of a Thiry-Vella fistula of the upper iutestine in antrectomized dogs caused distinct rise of acid secretion and after surgical removal of the fistula the secretion returned to levels observed after antrectomy only. This evidence indicates that isolated jejunal segment-induced acid hypersecretion can occur in the

absence of the antrum. Since Heidenhain pouches were used for these studies, the stimulus must be mediated by humoral substance (s) reacting directly on the parietal cells. All of these fingings relative to hypersecretion suggest that jejunal mucosa isolated from the mainstream of intestinal contents may release acid stimulant (s) responsible for the origin of hypersecretion. While our fingings appear to conflict with those of Nielson,[3] demonstrated that basal and pentagastrin-stimulated acid secretion, serum gastrin and gastrin in the antral mucosa were all significantly elevated in patients with a Roux-en-Y choledochojejunostomy compared to those of patients who had a choledochoduodenostmy. They concluded that the bypass of bile might introduce gastric hypersecretion to an altered biosynthesis and release of gastrin, whereas in ours it was not.

At least two different stimulatns can lead to hypersecretion observed in our model: histamine as noted by Menguy[1] and Silen,[8] enterooxyntin as indicated by Orloff[11] and Way.[12] Evaluation and elucidation of these possiblities must await further studies.

Bile diversion from the duodenum per se seems to be only one (and possibly not the most important) of the factors involved in increased gastric acid output when bile is routed into the intestinal tract through defunctionalized intestinal segments.

REFERENCES

1) Menguy RB: Mechanism of gastric hypersecretion in dogs with exclusion of bile of pancreatic juice from small intestine. *Surg Forum* **13**: 300, 1962.
2) Breen JJ. Molina E. Ritchie WP: Effect of common bile duct transplantation on gastric acid secretion in the dog. *Br J surg* **55**: 282, 1968.
3) Nielsen ML. Jensen SL. Malmstrom J. Nielsen OV: Gastrin and gastric acid secretion in hepaticojejunostomy Roux-en-y. *Surg Gynecol Obstet* **150**: 61, 1980.
4) McArthur MS. Longmire WP: Peptic ulcer disease after choledochojejunostomy. *Am J Surg* **122**: 155: 1971.
5) Kehne JH. Campbell RE: Choledochojejunostomy en Roux-Y study. *Arch Surg* **73**: 12, 1956.
6) Forrest JF. Longmire WP: Gastric hypersecretion after formation of small bowel conduit. *Ann Surg* **189**: 313, 1979.
7) Silen W. Hein MF. Albo RJ Harper HA: Influence of liver upon canine gastric secretion. *Surgery* **54**: 29, 1963.
8) Konturek SJ. Grossman MI. Enbahi GL: Effect of perfusion of intestinal loops with acid, fat, or dextrose on gastric secretion. *Gastroenterology* **49**: 48, 1965.
9) Nahrwold DL. Grossman MI: Effect of exclusion of bile from the intestine on gastric acid secretion. *Gastroenterology* **52**: 667, 1967.
10) Kerr G. Elliott DW: Effect of antrectomy on gastric acid hypersecretion induced by isolation of the proximal small bowel. *Am J Surg* **115**: 157, 1968.
11) Orloff MJ. Charters AC. Nakaji NT.: Further evidence for intestinal phase hormone that stimulates gastric acid secretion. *Surgery* **80**: 145, 1976.
12) Way LW. Cairns DW. Deveney CW.: The intestinal phase of gastric sacretion: a pharmacological profile of enterooxyntin. *Surgery* 77: 841, 1975.