

observation was based primarily on results with Methergine, a non-sympatholytic compound. Dibenamine evoked symptoms of central excitation which persisted for 30-45 minutes after injection though milk let-down was not inhibited in those animals who nursed during this period. Milk let-down, however, was significantly inhibited when the drug was injected 2 hours prior to nursing, after which time adrenergic blockade has occurred. Atropine induced a highly significant blockade of the let-down response when injected 150-220 minutes before nursing, but failed to block the response when administered 15-60 minutes before nursing. Oxytocin administered after any of these drugs restored normal milk let-down, indicating blockade was central rather than peripheral. Since Dibenamine, Hydergine and DHE 45 are powerful adrenergic blocking agents and atropine a cholinergic blocking agent, it is postulated both adrenergic and cholinergic links are present in the neurohumoral arc responsible for discharge of oxytocin from the posterior pituitary gland.

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Digestive Action of Gastric Juice Following Various Types of Gastric Resection for Duodenal Ulcer.* (23343)

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The present report evaluates operations designed for treatment of duodenal ulcer by comparison of the digestive action of the gastric juice following such procedures. For this purpose the erosive effect of gastric juice on the cat's esophagus has been measured and pepsin and acidity have been determined. These data have been compared with similar data from a study of control non-ulcer patients and another group of patients with un-

treated duodenal ulcer. Previous experiments (1) have shown gastric juice from 72% of untreated duodenal ulcer patients produced grade 3 to 5 digestion of the cat's esophagus during a 2 hour perfusion period. Only 9% of gastric specimens from control non-ulcer patients produced such severe degrees of esophageal erosion. Acidity and pepsin concentrations in the gastric juice of the majority of duodenal ulcer patients were found to be greater than in controls(1). A correlation of the data reported below, together with the observed incidence of ulcer recurrence following the several operative procedures studied

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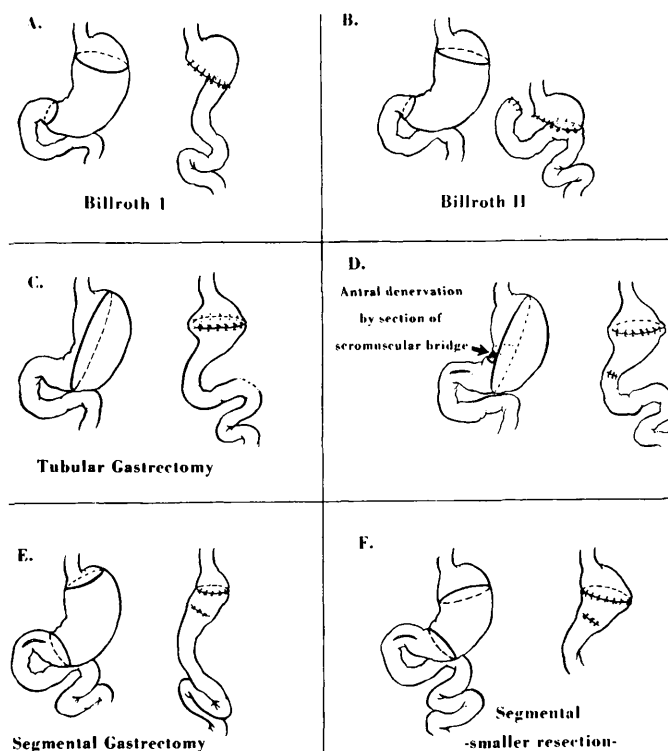


FIG. 1. Types of gastrectomy for duodenal ulcer.

suggests this method may prove to be one of the more precise and critical methods of evaluating the potential protective effect of an operation for duodenal ulcer.

Method. Patients who had undergone various types of gastric resection for duodenal ulcer were readmitted to hospital for overnight aspiration of the gastric contents. All operations had been done 3 months to several years previously. Secretions were collected by continuous suction from the gastric pouch with an inlying gastric tube from 11:00 p.m. to 7:00 a.m. The specimen bottle was kept on ice during the collection period, the volume was noted and the aspirate was then either frozen or subjected to analysis immediately. The pH was determined with a glass electrode and free HCl was determined by titration with 0.1 N NaOH. Pepsin was determined by the hemoglobin substrate method of Anson(2) and expressed as tyrosine activity units per cc of gastric juice. The gastric juice was adjusted to pH 1.6 to 1.7 with dilute HCl. The resultant solution was utilized to perfuse the esophagus of an anesthetized cat

as previously described(1). Degree of digestion of the esophagus at the end of a 2 hour perfusion period was graded after gross and microscopic examination. Grades 0, 1 and 2 represent slight to moderate erosion of the esophagus. Grades 3 and 4 indicate severe degrees of digestion; grade 5 represents perforation of the perfused esophagus.

Types of operative procedures studied are shown in Fig. 1. In both Billroth operations (A & B) a 75% excision of stomach including antrum had been done. Tubular gastrectomy (C)(3) entailed excision of the body and fundus with preservation of the cardia, lesser curvature and antrum. Reconstitution was by transverse gastroplasty. Heineke-Mikulicz pyloroplasty was done only if cicatricial stenosis of pylorus was present. Tubular gastrectomy with antral denervation(D) differed in that vagotomy at the level of the antrum was carried out by section of the narrow seromuscular bridge at the lesser curvature; pyloroplasty was then done routinely. The larger segmental gastrectomy (E)(4) entailed 85 to 90% excision of the acid-pepsin

TABLE I. Eight Hour Night Secretion Following Gastrectomy for Duodenal Ulcer.

Patients studied				Analysis of gastric aspirate									
Type of gastrectomy	No. of patients	Age		Sex		Vol (ml)		Free HCl (total mEq)		pH		Pepsin (units/ml)	
		Mean	Range	♂	♀	Mean	Range	Mean	Range	Mean	Range	Mean	Range
A. Billroth I	10	53	29-68	5	5	169	40- 510	1.0	0- 10.0	5.2	1.6-7.2	.6	1-2.0
B. " II	12	54	26-69	11	1	163	60- 321	0	0	5.7	3.5-7.4	.5	1-1.8
C. Tubular	20	52	27-73	11	9	360	80- 680	4.6	0- 37.4	3.9	1.6-6.0	.5	1-1.4
D. Tubular with antral denervation	6	62	31-77	4	2	292	80- 390	1.75	0- 10.5	4.3	2.1-7.0	.3	1- .6
E. Segmental (large)	11	52	30-68	9	2	354	45- 670	.2	0- 2.2	5.9	2.5-7.4	.2	1- .6
F. " (small)	21	50	24-76	17	4	316	10-1000	2.36	0- 35.0	4.7	1.2-7.0	.3	1- .8
G. Control (non-ulcer)	81	57	24-78	41	40	256	10- 800	3.04	0- 21.23	3.7	1.4-7.4	.9	1-5.0
H. Duodenal ulcer (untreated)	29	54	27-72	19	10	479	48-1100	19.04	0-110.40	2.1	1.2-4.2	1.7	2-4.1

TABLE II. Digestion of Cat Esophagus with Gastric Juice Obtained after Various Types of Gastric Resection for Duodenal Ulcer. Perfusion at pH 1.6-1.7.

Type of gastrectomy	Total No. of patients	Grade of digestion					
		With No. of patients whose gastric juice activity falls in each category					
		0	1	2	3	4	5
A. Billroth I	10	1	4	3	—	1	1
B. " II	11	4	4	1	1	—	1
C. Tubular	19	4	9	3	1	—	2
D. Tubular with antral denervation	6	2	3	—	1	—	—
E. Segmental (large)	11	1	8	2	—	—	—
F. " (small)	20	2	16	—	1	—	1
G. Control (non-ulcer)	56	15	30	6	2	2	1
H. Duodenal ulcer (untreated)	26	2	4	1	7	6	6

in the range of observations upon patients with active duodenal ulcer in only one instance; yet on perfusion, severe digestion of the cat esophagus followed in 3 instances. In 2 of these, gastric juice was obtained from patients known to have clinical evidence of recurrent ulcer. Persistent free hydrochloric acid in 30% of patients studied, and persistent high digestive activity of the gastric juice in 15% suggest that tubular gastric resection is not a suitable operation for duodenal ulcer.

D. Antral denervation added to tubular gastrectomy failed to provide uniform reduction in acid peptic digestive activity. One of 6 patients had a significant quantity of free HCl but perfusion of the cat's esophagus produced no erosion (grade 0). Digestive activity from the gastric juice of another patient in the series produced a grade 3 esophageal erosion. This group of patients is small; yet, the results suggest that an abnormal digestive potential was present in the gastric juice in at least one of them.

E. After the large segmental gastrectomy (85-90% excision of the acid-pepsin secreting area), the potential for ulceration by proteolytic digestion appears to be well controlled. In only one of 11 specimens studied was free HCl present and the value was small (2.2 mEq.). Pepsin values were low in all instances. Perfusion of the cat esophagus did not result in severe degrees of erosion in any instance.

F. With more limited excision of the acid-pepsin secreting area (40-60%), control of acid peptic digestion has not been as striking as following the larger segmental gastrectomy.

In 7 of 21 specimens, free HCl was present; in one of these because of the large volume (1,000 cc), the mEq. of free HCl was high, totalling 35. Pepsin concentration was not abnormally high in any instance, yet perfusion of the cat esophagus in 2 instances caused severe erosion (grades 3 and 5).

Discussion. The results of an assessment of the potential digestive power of gastric juice correlates well with our clinical experience with these operations in the surgical management of duodenal ulcer. The demonstration of significant acid peptic digestion by gastric juice of some patients studied after Billroth I and tubular operations is compatible with the known incidence of recurrent ulcer following these procedures (5,6). Although high levels of peptic digestive activity can be demonstrated in gastric juice after Billroth II resections, the pH of the juice is usually high due to continued mixing with the alkaline juices coming from the proximal duodenal loop. Thus pepsin activation is not great inasmuch as the pH is not optimal. In the Billroth II operation, therefore, one might reasonably anticipate fair protection against recurrent ulcer, largely through control of the pH. Extensive clinical experience with this operation indicates that the ulcer recurrence is in the area of 2 to 4%. In the large segmental gastrectomy (85-90% excision of acid-pepsin secreting area) uniform control of the acid peptic factor has been achieved in all patients studied. Clinical experience with this operation is comparable (4,7). Over one hundred patients have been followed 4 to 8 years following this operation without a single

recurrent ulcer. Patients having the smaller segmental gastrectomy (40 to 60%) have not been followed for a sufficiently long time to permit full clinical evaluation of the operation(7). No recurrent ulcer has yet been observed; however, significant acid peptic digestion in the gastric juice was observed in 2 of 20 patients (grades 3 and 5; 10%).

It is too early, therefore, to conclude that the smaller segmental gastric resection (40 to 60%) will protect against recurrent ulcer in the same measure as the larger segmental resection.

Summary and conclusions. Measurements of acid and pepsin values and determination of degree of digestion attending perfusions of the cat esophagus with gastric juice, obtained from patients after gastric resection for duodenal ulcer, have been made. These results indicate that esophageal perfusion employing the gastric juice of patients previously operated upon is a sensitive method for evaluating the likely protective effect of such operations against recurrent ulcer. Following procedures known to be associated with recurrent ulcers, gastric juice from some patients can be shown to have proteolytic digestive power not unlike that seen with untreated duodenal ulcer. After operations known from clinical experience to protect fully against recurrent ulceration,

the gastric juice of patients uniformly shows acid peptic digestion in the range of normals. This technic of assessment indicates that the protection afforded by some gastric resections is inadequate and that recurrence is likely to follow. The operation affording the greatest protection is definitely the larger (85-90%) segmental resection. Lesser grades of protection appear to be provided by the smaller (40-60%) segmental resection and the Billroth II procedure. Next in line would appear to be the protection afforded by tubular resection with antral denervation. Least protection against recurrent ulcer would appear to be afforded by tubular gastric resection and the Billroth I operation.

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Convulsions and Bizarre Behavior in Monkeys Receiving Chlorpromazine. (23344)

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That chlorpromazine may have convulsant actions in addition to its "tranquilizing" properties is suggested by a number of reports in the literature. Thus, in patients with epilepsy, Bonafede(1) reported that although addition of chlorpromazine to the therapeutic regimen without change in anticonvulsant medication did not augment seizure rates, reduction of the dosage of anticonvulsant drugs while chlorpromazine was being given was followed by an increased number of seizures in 26 out of 78 patients, one of whom died in status

epilepticus. Bente and Itil(2) observed that intravenous injection of 50 mg of chlorpromazine augmented paroxysmal activity in the electroencephalograms of epileptic patients, and in one of their subjects a major seizure occurred later. Likewise, Kopeloff *et al.*(3) found that, in monkeys with focal cortical cicatrices produced by topically applied discs of alumina cream, intravenous injection of 2 or 10 mg/kg of chlorpromazine accentuated focal spike and sharp wave electroencephalographic activity, and on some occasions also