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Digestive Action of Human Gastric Juice.* (22439)

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Perfusion experiments carried out by a number of workers(1-3) have shown the digesting and ulcerating effects of hydrochloric acid-pepsin solutions on living tissues, and the importance of pepsin in the production of such digestion has been emphasized. Dameron and Wangensteen(4) demonstrated the greater necrotizing effect in intestinal loops of canine gastric juice obtained from vagally innervated pouches under pilocarpine stimulation than that from Heidenhain pouches stimulated by histamine. The more severe degrees of damage produced by the former were assumed to be due to a greater peptic activity. However,

we have found no reference to the study of the peptic activity of human gastric juice by perfusion experiments of this type.

The present investigation was carried out to determine the digestive action *in vivo* of human gastric juice with simultaneous measurement of peptic activity and acidity. The results indicate that the gastric secretions of patients with duodenal ulcer, patients who are acutely ill, and patients in the early post-operative period secrete gastric juice with a greater digestion power than that of control patients and that this increased digestive action is due to increased peptic activity of the juice.

Method. Gastric secretion was collected from fasting patients by an inlying gastric tube

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TABLE 1. 8 Hour Night Secretion of Gastric Juice of Patients in Different Categories.

Category	Total No. of patients	Peptic activity										pH	% patients with pH 2.0 or below
		Volume (cc)		Free HCl (total Meq.)		Tyrosine units/cc		Pepsin,* mg/cc		Mean			
		Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range		
Control	53	263	10- 860	2.87	0-19.05	1.0	.1 -5.0	.55	.06-1.85	3.9	1.6-6.8	16%	
Duodenal ulcer	18	467	48- 960	20.90	0-63.65	1.7	.15-4.1	.89	.08-1.68	2.3	1.6-4.2	53	
Gastric "	9	384	90- 750	21.89	0-60.0	1.4	.24-3.0	.75	.14-1.4	2.7	1.4-6.7	50	
Acutely ill	9	549	240-1310	15.50	0-78.6	1.6	.55-2.4	.85	.29-1.19	2.4	1.0-4.0	63	
Postoperative	64	313	40-1100	7.60		1.4	.1 -5.2	.75	.06-1.87	3.8	1.5-7.7	29	
Gastric cancer	16	224	5- 850	.84	0-13.0	.6	.1 -1.8	.32	.06-.95	5.4	1.7-7.6	6.7	

* Expressed as mg/cc, 3 X crystallized bovine pepsin.

attached to a water siphon. The collecting bottle was kept on ice during the 8-hour period of aspiration from 11 p. m. to 7 a. m. The volume was measured and a sample removed for pH, acid, and pepsin determination. The pH was measured by the Northrup and Leeds glass electrode, pepsin was determined by the hemoglobin substrate method of Anson(5); free acid was measured by titration with .1 N NAOH. The pH of the remainder was adjusted to 1.6-1.7 with hydrochloric acid to provide an optimal medium for peptic activity. It was then used to perfuse the esophagus of the living anesthetized cat. The extensive susceptibility of the cat esophagus to the digestive action of gastric juice was demonstrated by Ferguson and associates(6). The sample was used for perfusion immediately or preserved below 0°C until used. Cats were anesthetized with pentobarbital (30 mg per kg) and a cannula was tied into the cervical esophagus and another into the gastric cardia. Perfusion of the cat's esophagus was carried out by dripping the gastric juice from a reservoir bottle at a rate of 25-35 ml per hour. The outflow tubing was raised to 20 cm above the level of the esophagus to provide a constant intraesophageal pressure. At the end of a 2-hour period the animal was sacrificed and the esophagus carefully examined. The degree of necrosis of the esophagus was graded as follows on the basis of gross and microscopic examinations: Grade 0: No injury or only hyperemia of the esophageal mucosa; Grade 1: Erosion of mucosal epithelium; Grade 2: Ulceration into submucosa; Grade 3: Digestion into muscular layers of esophagus; Grade 4: Impending perforation; Grade 5: Perforation during the perfusion period. Patients whose gastric secretions were studied were divided into the following groups: a) *Controls*: Patients admitted to hospital who were not acutely ill and who did not have duodenal ulcer, gastric ulcer or other gastric disease. b) *Duodenal ulcer*: Patients hospitalized on the Medical or Surgical Service for treatment of duodenal ulcer. All had clinical and radiographic evidence of active duodenal ulcer. c) *Gastric ulcer*: Patients hospitalized for treatment of

TABLE II. Results of Perfusion of Cat Esophagus with Human Gastric Juice.

Category	Total No. of perfusions	Grade of digestion					
		0	1	2	3	4	5
Control	32	5	19	5	1	1	1
Duodenal ulcer	18	1	3	1	3	5	5
Gastric "	9	1	5	2	—	—	1
Postoperatives	54	4	22	14	3	1	10
Acutely ill	7	—	1	1	4	—	1
Gastric cancer	9	2	5	2	—	—	—
HCl in distilled water, pH 1.6	5	4	1	—	—	—	—

a gastric ulcer believed to be benign. All except one of the group subsequently were operated upon and were shown to have a benign gastric ulcer. The remaining patient refused operation. d) *Gastric cancer*: Patients later demonstrated to have gastric carcinomas by operation. e) *Acutely ill*: Patients who, by clinical criteria, were known to be acutely ill at the time of gastric aspiration, but had not been operated upon recently, and did not have duodenal ulcer or a gastric lesion. (f) *Post-operative*: Patients who had undergone major extragastric surgical procedures one to 5 days prior to the period of gastric aspiration.

Results. Table I shows the results obtained by analysis of 8-hour night secretions for volume, free HCl, pepsin, and pH. Mean volumes were increased above control levels to a significant degree only in duodenal ulcer and acutely ill patients.

Peptic activity, expressed as tyrosine units (5), was significantly increased in the gastric secretions of patients with duodenal ulcer, and patients in the postoperative period. The mean value obtained for the acutely ill group is increased above control level, but is not significant ($t = 1.683$ $p = .1$). There was no significant difference in peptic activity in gastric juice of gastric ulcer and gastric cancer patients as compared with control values.

Mean pH values were significantly lower than the control value in the duodenal ulcer, gastric ulcer, and acutely ill patients. In addition, a greater percentage in each of these groups and the postoperative group had pH values optimal for peptic activity (pH 2 or below).

Table II shows the results obtained by per-

fusion of the cat esophagus with the gastric juice obtained from patients in various categories. Each perfusion was carried out with gastric juice of a different patient. Fig. 1 illustrates minimal (Grade 1) and severe (Grade 5) esophageal digestion produced by 2 hour perfusion. Gastric secretion from the majority of control patients produced only lesser degrees of esophageal damage. However, secretions obtained from 72% of patients with duodenal ulcer produced Grade 3 to 5 esophageal digestion. Likewise, the gastric secretions from patients in the early postoperative period caused greater esophageal digestion than normal. In this group 26% of specimens caused moderate to severe esophageal damage. Gastric aspirate from acutely ill patients shows a similar increased digestive power of the gastric juice. The differences in digestive action of gastric juice of patients in these three categories are significant as compared to that of controls. Except for one patient, gastric juice from persons with gastric ulcer caused no greater digestion of the cat's esophagus than that of control patients. Additional observations will be made upon patients with gastric ulcer as they become available for study. Gastric secretions obtained from persons with gastric cancer showed no variation in necrotizing effects from that of control patients.

Discussion. The finding of an increased digestion action on living tissue by the gastric secretions of duodenal ulcer patients is in agreement with data obtained from *in vitro* studies which have shown increased peptic activity in the gastric juice (7-9). However, although the number of patients available thus far has been small, results obtained suggest that gastric ulcer is not associated with increased digestive power of the gastric secretions. This would favor the concept that the pathogenesis of gastric ulcer and that of duodenal ulcer differ from each other.

The increased necrotizing action caused by gastric juice of acutely ill patients and patients in the early postoperative period supports the idea that ulcers of the upper gastrointestinal tract occurring during such stress periods are the result of increased proteolytic

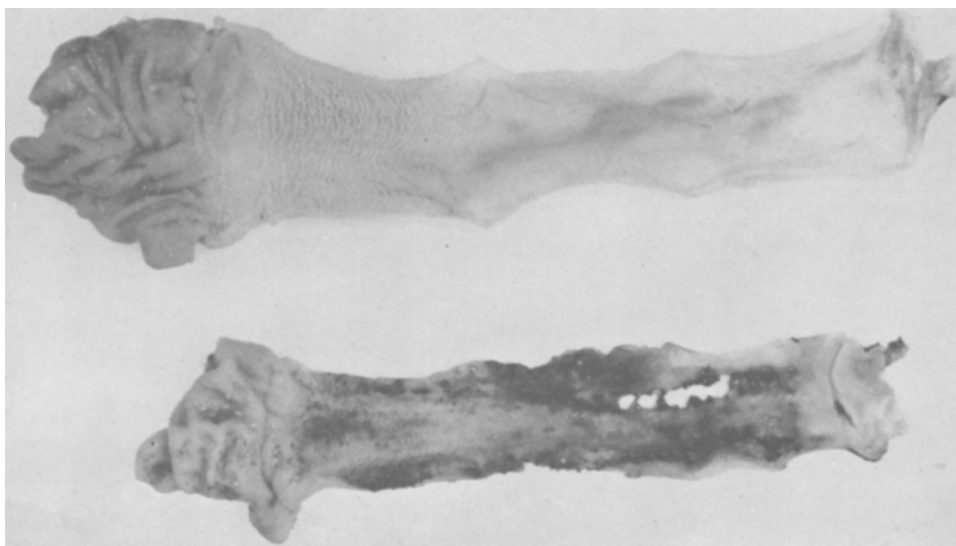


FIG. 1. (Upper): Grade 1 digestion of cat esophagus. Gastric juice from control patient. (Lower): Severe digestion and perforation of esophagus (Grade 5). Gastric juice from duodenal ulcer patient.

activity of the gastric juice rather than a decreased resistance of the mucosa of the intestine to ulceration. The results are in accord with the observations of Gray(10) and others that stress is accompanied by increased peptic activity of the gastric secretions. In addition, an optimal acid medium for peptic activity(2) is present in a greater proportion of the gastric secretions obtained from patients of these 2 groups.

Summary. 1. The digestive capacity of human gastric juice, adjusted to pH 1.6-1.7, has been measured by perfusion of the cat's esophagus. 2. The gastric secretions of patients with duodenal ulcer, patients in the early postoperative period, and acutely ill patients showed significantly increased necrotizing effects on the esophagus as compared with controls. Gastric secretions from patients with gastric cancer and benign gastric ulcer showed no such increased digestive activity. 3. Peptic activity measured *in vitro* was significantly increased in duodenal ulcer patients and patients in the postoperative pe-

riod. The mean pH values were significantly lower than control values in duodenal and gastric ulcer patients, postoperative patients and acutely ill patients.

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