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Inhibition of Gastric Secretion in the Rat By Normal and Abnormal Human Gastric Juice.* (26066)

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Human gastric juice contains an unidentified substance which, when injected intravenously, inhibits gastric secretion in the dog and in the rat(1,2). Brunschwig and associates found that gastric juice collected from patients with gastric cancer had a greater inhibitory effect on canine gastric secretion than that collected from normal individuals (3). Previously we reported that intravenous injection of normal human gastric juice consistently suppressed gastric secretory activity of pylorus ligated rats(4). Because of the small total doses of gastric juice required to produce inhibition and the possibility of conducting many experiments in a short period of time, the pylorus ligated rat appeared to be a good preparation for assaying inhibitory activity of human gastric juice collected under various conditions. The present report, using pylorus ligated rats, is concerned with comparison of gastric inhibitory activity of normal human gastric juice with that of gastric juice from patients with duodenal ulcer and gastric cancer.

Materials and methods. Gastric juice was collected from hospital patients either free from gastrointestinal disease or with proven duodenal ulcer or gastric cancer. Because of the relative scarcity of gastric cancer patients, juice from these patients was processed individually and pooled later in lots of 3. Processing of gastric juice and methods of studying effects of gastric juice material on gastric secretory activity in rats have been described (4). Control rats were given intravenously 1 ml of normal saline; test rats received 6 mg/200 g of normal human gastric juice preparation, cancer juice preparation, or ulcer juice preparation in 1 ml of normal saline. Experiments were performed in series of 20 rats with 5 rats each of control and 3 test groups. The mean 4 hour output of HCl in milliequivalents of each test group was compared with that of control group. Initially 60 rats were studied in this fashion. Several months later the same experiments were repeated on 60 rats of a different colony and with gastric juice material from different pools.

Results. The data from the 2 series of experiments are outlined in Table I. In rats receiving 6 mg of normal human gastric juice preparation, there was 85% and 79% inhibition of 4 hour output of HCl as compared to control rats receiving saline. In both experimental series there was even greater inhibition in rats receiving juice from peptic ulcer patients. On the other hand, although carcinoma juice caused in both experimental series significant suppression of secretory activity, degree of inhibition was less than that produced by normal juice. Statistical analysis of the data showed that in both series of experiments the means of test groups were significantly different than those of control groups. Moreover, means of the "ulcer group" and "normal group" were significantly different ($p<.001$ in Series 1 and $p<.05$ in Series 2). Means of "normal group" and

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TABLE I. Effects of Gastric Juice from Normal Patients and from Patients with Gastric Carcinoma and Duodenal Ulcer on 4-Hour Gastric Secretion in Pylorus Ligated Rats.

	Controls, 1 ml saline	"Normal" juice, 6 mg/200 g	"Ulcer" juice, 6 mg/200 g	"Carcinoma" juice, 6 mg/200 g
SERIES 1	16 rats	16 rats	15 rats	16 rats
4 hr output of free HCl in meq	.509 ±.254*	.075 ±.063 p <.001	.030 ±.026 p <.001	.255 ±.223 p <.01
% deviation from controls		−85%	−94%	−50%
SERIES 2	15 rats	14 rats	14 rats	14 rats
4 hr output of free HCl in meq	.392 ±.322	.081 ±.089 p <.001	.029 ±.031 p <.001	.106 ±.083 p <.01
% deviation from controls		−79%	−92%	−73%

* Mean and S.D. p = probability of significance of T value.

"cancer group" were significantly different only in the first series of experiments ($p<.01$ in Series 1 and $p<.20$ in Series 2). Means of "ulcer group" and "cancer group" were significantly different in both series of experiments ($p<.001$ in Series 1 and $p<.01$ in Series 2).

Discussion. Our data indicate that the active principle in human gastric juice responsible for inhibition of gastric secretion when given intravenously to rats is present in larger amounts or in a more active form in gastric juice from duodenal ulcer patients than in juice from normal individuals. On the other hand, this principle appears to be present in slightly lesser amounts or in a slightly less active form in gastric juice from individuals with gastric cancer. These results differ from those of Brunschwig and associates who found that gastric juice from patients with gastric cancer had greater inhibitory activity than juice from normal individuals(3). These investigators were injecting whole gastric juice in equal volumes, whereas in the present study equal weights of dialyzed, lyophilized juice were used. Gastric juice from patients with gastric cancer contains considerably more mucin per unit volume of water than does normal gastric juice. Therefore, it is likely that Brunschwig's results are explainable by much larger doses of the inhibitor substance in the dogs given carcinoma juice.

Assuming that this inhibitory principle has a physiologic role, it would appear that peptic ulcer disease is not due to a deficiency of this substance since it is found in peptic ulcer juice in greater amounts than in normal juice. However, since there is some evidence showing that the inhibitor is elaborated in the antrum(5), the greater inhibitory activity of peptic ulcer juice is in accordance with the fact that antral inhibition of gastric secretion is enhanced by hyperacidity of the antral contents. Conversely, one would expect to find less inhibitory substance in gastric juice under conditions of achlorhydria, as accompanying gastric cancer. However, the assumption that the inhibitory substance in human gastric juice, demonstrable by animal secretion studies, has a physiologic role in man has yet to be proven.

Summary. Intravenous administration of dialyzed, lyophilized gastric juice from normal subjects, patients with peptic ulcer and patients with gastric carcinoma, induced pronounced depression of secretion of hydrochloric acid and water in the pylorus ligated rat. Peptic ulcer juice had the greatest inhibitory effect, whereas gastric carcinoma juice had the least.

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