Excretion of 5-Hydroxyindoleacetic Acid Following Bowel Ischemia in Dogs. (26065)

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Since the major part, perhaps 90-95%, of the body's serotonin (5-hydroxytryptamine) is located in the gastrointestinal mucosa(1), this study was designed to determine whether production of severe intestinal ischemia in dogs would influence urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA), the end product of serotonin metabolism.

Method. Fasting greyhound dogs of both sexes, weighing between 22 and 32 kg with an average weight of 25 kg, were used. Three experiments were performed utilizing 4 animals in each experiment. Following production of general anesthesia with intravenous pentobarbital sodium, an intravenous infusion was initiated which ran throughout the 6 hour test period. The infusion delivered approximately 7 to 8 cc of 5% dextrose in water/kg body weight/hr. The bladder of each animal was catheterized, the first sample of urine discarded, and urine collected hourly thereafter. The 5-HIAA content of each urine sample was determined by the method of Udenfriend *et al.*(2). In all animals, urine was collected for 2 hours before any procedures were performed. Then 2 test conditions and 2 controls were established as follows: 1) Control Group: Laparotomy only (3 animals). 2) Control Group: Laparotomy and ligation of terminal aorta producing ischemia of the hind quarters (3 animals). 3) Test Group: Laparotomy and ligation of the arterial supply to the mesenteric small bowel followed by strangulation of the mid 2 feet of small intestine by a cord (6 animals). Following institution of test or control conditions, urine specimens were collected for an additional 4 hours.

Results. Mean basal excretions of 5-HIAA are shown in Column 1 of Table I. Statistical evaluation utilizing an analysis of covariance reveals f value of 1.67 which for 3 and 8 degrees of freedom is not significant at the 0.05 level. This indicates that there was no initial difference between animals tested.

TABLE I. Mean Hourly Excretion, mg/Hr, of 5-Hydroxyindoleacetic Acid.

	Mean hourly amounts (mg) in 3 groups		
	Test control		Test
Basal excretion	Laparotomy	Aorta ligation	bowel ischemia
.55	.33		
1.10	.46		
.75	1.93		
1.45		.26	
.46		.24	
.36		.53	
.40			.11
.40			.16
1.20			.40
1.60			1.25
.41			.31
.73			.63

During the subsequent 4 hours' excretion of 5-HIAA, within-group variation was greater than between-group variation, consequently a probability value could not be determined (Table I). This indicates, however, that post operative differences were not significant. Using the preoperative values to predict what would be expected, statistical results revealed a f of 2.15 which suggests that some changes occurred, but were not great enough to be significant. Neither was there a significant difference between test and 2 control groups.

Conclusions and summary. Although it is not possible to determine the effect of ischemia on serotonin contents of bowel mucosa by this experiment, urinary excretion of 5-HIAA in large dogs does not change in the first 4 hours after production of severe bowel ischemia.

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1. Sjoerdsma, A., *New England J. Med.*, 1959, v261, 181.

2. Udenfriend, S., Weissbach, H., Brodie, B. B., Assay of Serotonin and Related Metabolites, Enzymes, and Drugs, Methods of Biochemical Analysis, Interscience Publishers, N. Y., 1958, v6, 95.

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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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