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Antral Inhibition of Gastric Secretion.* (22982)

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Edkins(1) proposed that presence of secretagogues in the stomach promoted gastric secretion by release of a hormone, "gastrin," from the antral mucosa. Although his experiments were inadequate to prove this hypothesis, subsequent studies have demonstrated that the gastric phase of gastric secretion is mediated by a hormonal mechanism which is initiated by chemical(2) and mechanical(3) stimulation of the antral mucosa. The presence of acid of sufficiently strong concentration within the antral portion of stomach will diminish the rate of gastric secretion which results when antral gastrin mechanism is stimulated by secretagogues within the antrum(4). Whether the acid environment is unsuitable for release of gastrin or whether it results in production of a substance which actively inhibits production of HCl is not clearly established. Woodward (4), interested in the possible existence of a gastric secretory inhibitor factor from the antrum, was unable to inhibit the secretory effect of histamine by perfusion of the isolated, innervated antrum with acid and concluded that such a factor did not exist. Recently Harrison *et al.*(5) utilizing the technic of a divided antrum have presented evidence for existence of a gastric secretory inhibitor mechanism within the antrum. We have attempted to prove the existence of this mechanism by using the divided antral pouch technic in such a way that the environment of each antral segment may be altered simultaneously at will.

Method and procedure. Four healthy adult mongrel dogs were prepared as follows: The gastric antrum was removed from the gastrointestinal continuity and divided longitudinally forming 2 small antral pouches which were marsupialized. A Heidenhain pouch was constructed and drained by a

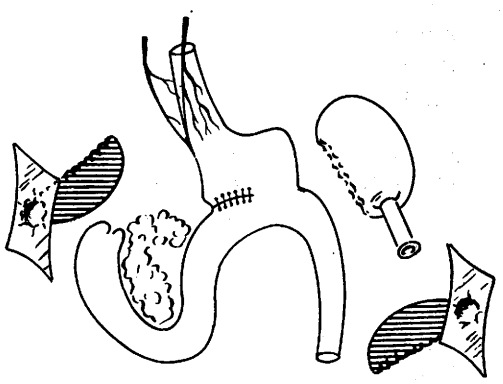

FIG. 1. Experimental preparation of stomach consisted of a Heidenhain pouch, 2 marsupialized antral pouches and a gastrojejunostomy.

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stainless steel cannula for collection of gastric juice. Gastrointestinal continuity was restored by gastrojejunostomy. A wedge of the stomach between antrum and fundus was discarded to insure against the presence of antral mucosa in the Heidenhain pouch or acid secreting cells within the antral pouches. The final preparation is represented by Fig. 1. After recovery periods of 3 weeks, the animals were subjected to the following study. After a 12 to 16 hour fast, a dog was placed in a Pavlov frame and gastric juice was collected from the Heidenhain pouch every 30 minutes. Following 2 control periods, perfusion of 10% alcohol, used as stimulant for gastric juice secretion(6) was begun, in either of the antral pouches and was continued in the same pouch throughout remainder of experiment. After a sustained secretory response was obtained with alcohol, perfusion of 0.1N HCl was begun in the other antral pouch. Perfusion of alcohol in the first pouch and acid in the second pouch was continued until the HCl response from the Heidenhain pouch was completely or significantly inhibited. In all but 2 experiments which demonstrated inhibition of gastric secretion, physiological saline was substituted for perfusion of acid as the third phase of the study. Perfusions of alcohol and saline were continued to see if the secretory response to alcohol would return. The free HCl in gastric juice was titrated with 0.1N NaOH with Toeppfer's reagent as indicator. The amount of free HCl for each collection period was expressed in milliequivalents (mEq).

Results. Twenty-nine experiments were performed on 4 dogs. Alcohol failed to initiate gastric secretory response in 6 studies, (5 of these occurred in 1 dog). These experiments were terminated and are not considered in this analysis. In 17 of the remaining 23 studies, secretory response to perfusion of alcohol in one antral pouch was inhibited by perfusion of HCl in the second antral pouch. A perfusion of saline was substituted for perfusion of acid in 15 of the 17 experiments exhibiting gastric secretory inhibition. A return of free acid or an increase in acid secretion occurred in 10 of these studies. The 5 experiments that failed to demonstrate a significant return of gastric secretion occurred in 1 dog.

TABLE I. Mean HCl Production in mEq for Last 2 Periods of Each Experimental Phase.

Dog		I Alcohol	II Alcohol-acid	III Alcohol-saline
I	1	.15	.08	.63
	2	.40	.10	.25
II	1	1.73	.14	.85
	4	.10	.02	.09
	6	.69	.02	.10
III	1	.42	.05	.37
	2	.85	.02	.10
	3	1.12	.08	.44
	4	.13	.01	.20
IV	1	1.69	.24	0
	2	.07	0	.26
	4	1.40	.03	0
	5	.15	.02	.01
	7	.38	.03	0
	8	1.48	.02	.01

Five of the 23 experiments, demonstrating an initial secretory response to alcohol, failed to display gastric secretory inhibition when perfusion of the second antral pouch with hydrochloric acid was performed.

The magnitude of the response to alcohol stimulation or acid inhibition was not related to the antral pouch employed for these perfusions except when there was a marked discrepancy in size. Then, the magnitude of alcohol secretory response and the acid inhibitory response depended upon whether the large pouch was employed for alcohol or acid perfusion respectively.

To analyze the results statistically, the average HCl output for the last 2 periods of each of the 3 phases of an experiment was considered the maximum secretory or inhibitory response obtained for the respective

TABLE II. Analysis of Variance between Phases I, II, and III.

Source of variation	Degrees of freedom	Sum of squares	Mean square	F	P
Between phases of exp.	2	3.59	1.79	20.8	<.01
Between exp.	14	2.50	.18		
Discrepance	28	3.77	.086		
Total	44	9.86			

TABLE III. Mean HCl Production in mEq for Last 2 Periods of Experimental Phases I and II.

Dog		I Alcohol	II Alcohol-acid
I	1	.15	.08
	2	.40	.10
	3	.64	.02
II	1	1.73	.14
	2	.10	.09
	3	.42	.60
	4	.10	.02
	5	.25	.50
	6	.69	.02
III	1	.42	.05
	2	.85	.02
	3	1.12	.08
	4	.93	.61
	5	.13	.01
	6	.42	.57
IV	1	1.69	.24
	2	.07	0
	3	1.10	1.13
	4	1.40	.03
	5	.15	.02
	6	.44	.09
	7	.38	.03
	8	1.48	.02

phases. Thus expressed, the data for the 15 experiments in which all 3 phases of study were performed, are seen in Table I. In Table II the analysis of variance of these data indicates that there is a significant difference in HCl production between the 3 phases of the experiment ($P<.01$). In a similar manner, the data for phases 1 and 2 of all 23 experiments are tabulated in Table III and the analysis of variance of these data (Table IV) indicates that there is a significant difference in gastric secretion between these two phases of the experiment ($P<.01$).

Discussion. Evidence presented by Harrison *et al.*(5) suggests that the antrum may actively inhibit production of gastric HCl which is mediated by chemical stimulation of the antral gastrin mechanism. The evidence presented by these authors suggests the hypothesis that reduction of pH within the antrum may actively inhibit gastric secretion by liberation of an inhibitory substance. The results of the present study using the double antral pouch preparation described above, provide direct evidence to support this hypothesis. In 17 of 23 experiments reported, the antral gastrin mechanism initiated by perfusion of one antral pouch with alcohol was inhibited by perfusion of the second antral pouch with HCl.

TABLE IV. Analysis of Variance between Phases I and II of All Experiments.

Source of variation	Degrees of freedom	Sum of squares	Mean square	F	P
Between phases of exp.	1	2.44	2.44	15.25	<.01
Between exp.	22	4.53	.206		
Discrepance	22	3.57	.16		
Total	45	10.53			

The time required to inhibit the antral gastrin mechanism with antral perfusion of HCl varied from 1 to 3 hours. The reason for the wide variation in time to initiate the inhibitory mechanism is not clear. It has been our opinion that strength of the antral gastrin mechanism and the antral inhibitor mechanism may be dependent upon size of antral pouch perfused with alcohol and acid respectively.

The demonstration that gastric secretion is inhibited by antral perfusion with HCl can best be interpreted as the result of a humoral mechanism. It is our opinion that this mechanism is of a hormonal nature; however, further studies are required to elucidate this question. The importance of the gastric secretory inhibitor factor in the control of HCl production in normal and pathological states must be evaluated.

Summary. A method has been devised for making a Heidenhain pouch and 2 separate, marsupialized, antral pouches in the dog. Studies performed on 4 dogs prepared in this way indicate that reduction of pH within one antral pouch will inhibit production of HCl in the Heidenhain pouch when the latter is under stimulation by perfusion of alcohol in the second antral pouch. It is assumed that gastric inhibition produced in this manner demonstrates release of an inhibitory hormone by the antrum; however, this awaits further study for clarification.

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Different Fractions of Plasma Proteins in Some Infectious Diseases. (22983)

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Changes in plasma protein patterns usually manifest themselves by increase or decrease in concentrations of normal components or by appearance of protein fractions not seen under normal conditions. Different fractions of plasma proteins have been determined in different diseased conditions(1-6) but such studies in patients suffering from acute infectious diseases like cholera, small pox, tetanus and meningitis have not been published. The present communication deals with such studies in patients suffering from cholera, tetanus, small pox and meningitis by paper electrophoresis. Similar studies were also carried out in normal Indians for comparison.

Methods. Blood samples were collected in vials, containing crystals of potassium oxalate, from the anticubital vein as soon as patients suffering from small pox, tetanus and meningitis were admitted to the hospital. In patients suffering from cholera, blood samples were withdrawn when dehydration of the body was controlled by transfusion of saline and patients had normal urination. Normal subjects were students of our department of physiology. Total nitrogen in .1 cc plasma and nonprotein N in tungstic acid blood filtrate equivalent to 0.5 cc plasma were determined by the micro-Kjeldahl method. By multiplying the difference between the total N and nonprotein N with 6.25, total protein value of blood plasma was obtained. Fibrinogen was determined in 1 cc plasma by isolation as fibrin according to the method of Cullen and Van Slyke(7) and determination of N in fibrin by the micro-Kjeldahl method. 1 cc plasma was diluted 3 times with barbiturate-barbituric acid buffer of pH 8.6 and ionic concentration .05. .02 cc of the dilute plasma was applied to paper strip and electrophoretic separation was carried out for 12 hours by using L.K.B. paper electrophoresis apparatus with current of 6 mA and 300 volts. The filter paper strips were dried at 100°C, immersed in .1% bromophenol blue in absolute ethanol saturated with mercuric chloride for 30 minutes, washed in .5% acetic acid, dried, optical density curves of the different colored zones plotted using Photovolt Photoelectric Densitometer Model 425 on graph paper, and areas of component sections of graph were measured by cutting out the curves and weighing in micro balance. Total area of plotted curve was equivalent to total plasma protein content of sample used for electrophoresis, determined by the micro-Kjeldahl method. Weight of component sections of curves was proportional to area and protein value of each component was calculated from total protein value. As γ-globulin and fibrinogen zones in the electrophorogram were almost inseparable, the former was determined by deducting the sum total of albumin, α-globulin, β-globulin and fibrinogen values from the total protein value. The results are given in Table I.