Maximal histalog test in control subjects and patients with peptic ulcer

KENNETH G. WORMSLEY AND MORTON I. GROSSMAN

*From the Veterans Administration Centre and University of California
School of Medicine, Los Angeles, California, U.S.A.*

EDITORIAL SYNOPSIS This is a very valuable detailed analysis of the maximal histalog test. The studies suggest that increased parietal cell mass in duodenal ulcer is unlikely to be the most important factor in its pathophysiology. It was noted that impaired secretory capacity suggesting mucosal damage is associated with peptic ulcer in a considerable proportion of patients of all categories.

Previous studies have established the dose of histalog required to produce maximal stimulation of acid secretion (Ward, Gillespie, Passaro, and Grossman, 1963; Zaterka and Neves, 1964). In the present investigation, maximal stimulation with histalog was used to compare gastric function in patients with peptic ulcer and in control subjects.

METHODS

Each patient to be tested was fasted overnight and in the morning had a tube (16F) passed through the nose. The position of the tube was checked fluoroscopically. The patient remained seated throughout the test. Saliva was expectorated when necessary. Gastric juice was aspirated continuously and mechanically at 30 mm. Hg sub-atmospheric pressure, with automatic switch-off for 10 out of every 60 seconds. All tests were performed by the same technician.

After removal of the residual juice, basal secretion was aspirated for one hour. Histalog (Betazole, 3-beta aminoethylpyrazole dihydrochloride, Lilly) was then injected subcutaneously in a dose of 1.5 mg. per kg. body weight. A dose of this order had been found to evoke maximal secretion in similar patients (Ward *et al.*, 1963) and in a recent report from Brazil (Zaterka and Neves, 1964). The stimulated secretion was aspirated in eight quarter hourly periods. In 12 subjects the whole test was done again within 14 days, in order to assess repeatability.

A sample of the aspirated juice was titrated electrometrically to pH 7.0, using 0.2N sodium hydroxide with an autoburette titrator and pH meter (Radiometer, Copenhagen, Denmark).

PATIENTS The patients were male veterans (Table I). The control group comprised patients from the surgical services who were suffering from inguinal hernias, varicose veins and other minor non-alimentary dis-

TABLE I
AGE DISTRIBUTION OF PATIENTS HAVING
MAXIMAL HISTALOG TESTS

	<30	30-39	40-49	50-59	60-69	≥70	Total
Controls	6	15	15	18	14	7	75
Duodenal ulcer	9	23	42	22	13	8	117
Duodenal + gastric ulcer	0	0	9	3	8	4	24
Prepyloric ulcer	1	4	10	8	10	2	34
Corpus ulcer	0	2	7	3	6	3	21
Total	16	44	83	54	51	24	272

abilities, and patients from the medical services admitted for investigation of epilepsy or convalescing from pneumonia and other miscellaneous non-alimentary illnesses. None of the control patients had ever had symptoms suggesting peptic ulcer.

Unequivocal clinical and radiological evidence was present in all patients with ulcer. Patients with gastric ulcer were classified radiologically into those with ulcers proximal or distal to a line dropped vertically from the incisura. To assess the influence of duration of illnesses, patients were considered to have 'acute' ulcers if their history was shorter than six months, and 'chronic' ulcers if symptoms had been present longer than five years. Subjects with symptoms of intermediate duration were designated as an 'intermediate' group (Table II).

STATISTICAL METHODS For purposes of comparison, the secretory response to histalog was expressed as peak 30 minute, peak 60 minute, and one and three quarter hour periods. The first quarter hour following the injection of histalog was omitted from the analysis because secretion during this period was very variable, presumably due to factors not related to gastric secretory function, such as rate of absorption from the site of injection. The peak concentration was the maximal acid concentration reached in any of the 15-minute samples. The mean concentration was the average concentration during the final seven periods after injection of histalog.

TABLE II

DURATION OF DISEASE OF PATIENTS WITH DUODENAL ULCER																	
<30			30-39			40-49			50-59			60-69			≥70		
a	i	c	a	i	c	a	i	c	a	i	c	a	i	c	a	i	c
2	2	5	5	3	15	6	2	34	5	2	15	5	3	5	2	0	6
a = acute ulcer (history less than six months); c = chronic ulcer (longer than five years); i = ulcers of intermediate duration.																	
Total			25			12			80								

The statistical significance of the difference in distribution of secretory values in the various groups or subgroups was determined by use of the Mann-Whitney 'U' test (Siegel, 1956). The upper limit of normal was determined by the method of Herrera (1958). Using the criterion that there be a 95% probability of excluding no more than 5% of normals, the required rank number turned out to be the highest observed value of our control group and this was therefore taken as cut-off point. This criterion for setting the upper limit of normal differs from the one used in previous studies (Grossman, 1960; Grossman, Kirsner, and Gillespie, 1963). Linear regression equations were determined by the method of Bartlett (1949), since both variables being analysed were subject to error.

In the text and tables, p values greater than 0.05 are considered not significant.

RESULTS

No patient in the control group or with peptic ulcer failed to respond to histalog. Repeatability of all indices of stimulated secretion was excellent (Table III). Repeatability was as good in patients with low output as in those with greater response (Fig. 1).

FIG. 1. Duplicate histalog tests in 12 patients, 11 with duodenal ulcer.

TABLE III

CORRELATION OF DUPLICATE SECRETORY DATA

Secretory Data	Correlation Coefficient (r)
Basal	
Output	0.58
Volume	0.62
Concentration	0.60
Histalog response	
30-minute output	0.93
30-minute volume	0.94
60-minute output	0.97
60-minute volume	0.96
One and three quarter-hour output	0.98
One and three quarter-hour volume	0.97
Peak concentration	0.95
Mean concentration	0.92

Duplicate basal secretion of 41 patients, comprising six controls, five patients with gastric ulcer and 30 with duodenal ulcer. Duplicate histalog tests in 12 patients, 11 of whom had duodenal ulcer.

CONTROLS Values for basal output and concentration were lower, but the response to histalog was greater (Table IV) than values in previously recorded studies of the augmented histamine test (Table V).

FIG. 2. Peak 30-minute response to histalog of controls and patients with duodenal ulcer, showing median values for each decade. The values for patients with duodenal ulcer below 30 years and above 60 years differ significantly from the remainder of the group.

TABLE IV

SECRETORY DATA FOR CONTROLS AND PATIENTS WITH PEPTIC ULCER

Secretary Data	75 Controls			117 Patients with Duodenal Ulcer			24 Patients with Duodenal + Gastric Ulcer			35 Patients with Prepyloric Ulcer			21 Patients with Corpus Ulcer		
	Mean	Median	Upper Limit of Normal	Mean	Median	Upper Limit of Normal	Mean	Median	Upper Limit of Normal	Mean	Median	Upper Limit of Normal	Mean	Median	Upper Limit of Normal
Basal Secretion															
Output (mEq.)	1.8	1.4	10.2	2.1	1.4	1	1.8	0.8	0	1.1	0.2	0	1.5	0.7	0
Volume (ml.)	58	50	240	64	60	1	50	40	0	50	38	0	50	41	0
Concentration (mEq./l.)	31	28	96	30	23	1	29	23	0	18	14	0	26	19	0
Stimulated secretion															
30-minute output (mEq.)	17.2	16.8	29.9	21.2	21.1	20	18.8	19.0	4	16.0	15.3	3	14.5	12.4	3
30-minute volume (ml.)	142	146	216	176	180	25	160	165	5	142	122	5	137	118	2
60-minute output (mEq.)	30.9	30.0	56.6	39.3	38.8	16	36.0	35.1	2	28.4	27.4	0	26.0	24.0	2
60-minute volume (ml.)	264	258	417	327	332	17	308	312	5	254	232	1	242	234	2
One and three-quarter hour output (mEq.)	47.6	46.4	89.6	61.7	60.6	15	57.3	56.1	2	44.3	42.4	0	40.2	38.8	2
One and three-quarter hour volume (ml.)	420	422	695	521	518	15	510	504	2	402	368	1	383	379	2
Mean concentration (mEq./l.)	109	120	146	116	117	1	116	117	1	108	109	1	96	96	0
Peak concentration (mEq./l.)	123	131	152	128	130	2	128	129	1	119	123	0	108	102	0

¹The figures in the control column indicate the appropriate values for this limit, calculated to exclude no more than 5% of the normal population ($p = 0.05$). The figures in the other columns indicate the number of patients with values above this level.

TABLE V

SUMMARY OF PREVIOUS STUDIES OF GASTRIC ACID SECRETION IN MEN

Reference	Basal Acid Output (mEq./hour)			Basal Volume (ml./hour)			Peak 30-min. Output (mEq.)			Peak 30-min. Volume (ml.)		
	Normal	Duodenal Ulcer	Gastric Ulcer	Normal	Duodenal Ulcer	Gastric Ulcer	Normal	Duodenal Ulcer	Gastric Ulcer	Normal	Duodenal Ulcer	Gastric Ulcer
Levin, Kirsner, and Palmer (1951)	2.6	6.0	2.3	79	110	81						
Lopes, Palmer, and Kirsner (1959)	2.0	5.3	1.3	75	117	192	6.0 ^{1,2}	10.0 ^{1,2}	7.0 ^{1,2}	78 ^{1,2}	110 ^{1,2}	96 ^{1,2}
Grossman (1960)	1.4	2.8										
Sircus (1960)	2.5	6.0	2.1				11.2 ²	18.8 ²	7.3 ²			
Baron (1963a, b, c)	1.3	3.6	1.9	39	62	45	10.8	21.0	11.3	107	176	118
Correia and Moura (1963)	4.0	11.5					8.1 ²	18.1 ²				
Grossman <i>et al.</i> (1963)	2.4	5.3	1.5				5.8 ^{1,2}	10.0 ^{1,2}	4.8 ^{1,2}			
Marks <i>et al.</i> (1963)	4.2	7.1	4.3				11.3 ²	17.6 ²	9.8 ²			
Present study	1.8	2.1	1.5	58	64	50	17.2	21.2	14.5	142	176	137

All values of stimulated secretion refer to the augmented histamine test, except those marked: ¹submaximal histalog (0.5 mg./kg. body weight), and the present study. ² $\frac{1}{2}$ maximal acid output.

None of the indices of acid secretion used in this study showed a significant age trend, thus differing from previous reports (Kirsner and Ford, 1955; Baron, 1963a; Grossman *et al.*, 1963) (Table VI and Fig. 2).

PATIENTS WITH DUODENAL ULCER Patients with duodenal ulcer older than 60 years secreted less than the remainder of the group (Table VI).

Basal secretory patterns of patients with duodenal ulcer were similar to the controls. An equal proportion (10%) of patients with duodenal ulcer and controls showed a poor response to histalog (less than 10 mEq. in 30 minutes), but patients with duodenal ulcer secreted significantly larger mean

volumes of gastric juice than the controls (Fig. 3) and a small, but significant proportion of patients with duodenal ulcer secreted more than any control subjects (Fig. 4 and Tables IV and VIII). Neither peak nor mean concentration of acid in patients with duodenal ulcer differed significantly from the control values.

The secretory patterns of patients with acute duodenal ulcers did not differ significantly from those with chronic ulcer (Table VII). Patients with chronic ulcers were divided into an 'intermittent' group with long intervals between symptoms and a 'recurrent' group with symptoms at least once a year and more than one period of hospitalization; a significantly higher mean acid output was found in

TABLE VI
INFLUENCE OF AGE ON GASTRIC SECRETORY RESPONSE

	Controls (21)		Duodenal Ulcer (21)		Prepyloric Ulcer (12)		Corpus Ulcer (9)	
	Median	P	Median	P	Median	P	Median	P
Basal output (mEq./hour)	1.3	n.s.	0.8	<0.001	0.3	n.s.	0.7	n.s.
Basal volume (ml./hour)	50	n.s.	29	<0.001	32	n.s.	34	n.s.
Thirty-min. output (mEq.)	14.8	n.s.	18.5	<0.001	15.5	n.s.	12.4	n.s.
Thirty-min. volume (ml.)	138	n.s.	142	<0.002	115	n.s.	100	n.s.
One and three-quarter-hour output (mEq.)	39.9	n.s.	50.0	<0.006	42.4	n.s.	43.6	n.s.
One and three-quarter-hour volume (ml.)	367	n.s.	430	<0.001	348	<0.004	346	<0.02

Figures in parentheses denote number of subjects aged 60 and over in each category and median values are for these subjects. 'P' values refer to differences between these patients and younger subjects in the same category.

patients with more severe symptoms, but both categories showed a wide range (Table VII). A history of haematemesis was not associated with acid output significantly different from the remainder of the patients with duodenal ulcer, but patients whose duodenal ulcer had perforated at some time had a significantly higher mean rate of acid secretion. The patients who required surgical treatment for duodenal ulcer had secretory tests carried out in connexion with another study, after a decision to operate had been made on clinical grounds, such as history of perforation, recurrent or persistent bleeding, or repeated admission to hospital. Mean peak response to histalog in this group was significantly greater than that of the unoperated patients with duodenal ulcer, but again the ranges overlapped.

PATIENTS WITH CONCURRENT GASTRIC AND DUODENAL ULCERS These patients had radiological findings diagnostic of both gastric and duodenal ulcers in studies done within 10 days of the secretory tests.

The secretory patterns were similar in all respects to patients with duodenal ulcer alone (Tables IV and VIII).

No difference in the response to histalog was found whether the gastric ulcer was situated in the antrum or in the body of the stomach.

PATIENTS WITH PREPYLORIC ULCERS Basal acid output, volume of gastric juice, and concentration of acid were lower in patients with prepyloric ulcer than in controls (Tables IV and VIII). However, following stimulation with histalog, secretory patterns were very similar in control subjects, differing only in lower mean concentration.

PATIENTS WITH ULCERS OF THE BODY OF THE STOMACH Both basal and stimulated secretion of acid of most of the patients with corpus ulcer was significantly less than for control subjects, due especially to lower concentration of acid in the gastric aspirate (Tables IV and VIII). However, some of the patients

FIG. 3. Mean values and standard errors for 75 control patients and 117 patients with duodenal ulcer during the basal hour and eight 15-minute periods of histalog test. The figures show the tendency for acid output to level off and then fall away in both groups of patients. The differences in acid output were attributable to the different volumes of gastric juice secreted by the two groups, since there was no significant difference in the concentration of acid during the course of the test. The low basal output in the two groups is due to the low basal acidity.

FIG. 4. Distribution of values of peak 30-minute acid output, showing marked overlap of all groups, tendency of patients with duodenal ulcer to secrete more than the controls, and separation into two subgroups of patients with corpus ulcers.

TABLE VII

BASAL AND PEAK 30-MINUTE ACID OUTPUT OF SUBGROUPS OF DUODENAL ULCER POPULATION

	No. of Patients	Basal Output (mEq.)		Peak 30-min. Output (mEq.)		P
		Range	Median	Range	Median	
Duodenal ulcer	117	0-16.5	1.4	3.1-48.5	21.1	— <0.01 <0.005
+ haematemesis	39	0-9.9	1.3	6.3-40.2	21.1	
+ perforation	13	0-10.1	2.2	7.3-35.7	24.4	
+ surgery	16 ¹	0-15.8	2.7	13.9-52.2	31.3	
Duodenal ulcer						0.13
Acute	25	0-4.3	0.8	3.1-36.6	18.8	
Chronic	80	0-16.5	1.4	6.3-48.5	21.5	0.024
Duodenal ulcer						
Intermittent	15	0-7.1	1.0	6.4-33.9	17.5	
Recurrent	26	0-16.5	1.8	7.3-36.1	23.0	

¹The only subgroup which is not from the consecutive series of 117 patients with duodenal ulcer in this study. The 'P' values indicate the significance of the difference of peak acid output for each subgroup compared with the first subgroup in each category.

with corpus ulcer had secretory responses greater than normal and comparable with the upper range of patients with duodenal ulcer (Fig. 4).

DISCUSSION

The basal output in both controls and patients with duodenal ulcer was considerably lower in this study and in a previous study from this hospital (Grossman

1960) than in other reports from America, Europe, or South Africa (Table V). We are unable to explain this discrepancy, which is perhaps due to our selected population. Satisfactory recovery of gastric juice was demonstrated with phenol red marker; moreover, the volumes of basal secretion were similar to values reported in other studies, while the volumes of gastric juice after stimulation were considerably greater than in previous reports

TABLE VIII
PROBABILITY VALUES OF DIFFERENCES IN GASTRIC SECRETORY DATA FROM SPECIFIED GROUPS OF SUBJECTS

	Basal Output	Basal Volume	30-Min. Output	30-Min. Volume	60-Min. Output	60-Min. Volume	One and Three-quarter-Hour Output	One and Three-quarter-Hour Volume	Peak Concentration	Mean Concentration
Control < duodenal ulcer	n.s.	n.s.	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	n.s.	n.s.
Control > prepyloric ulcer	<0.001	<0.01	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	<0.01
Control > corpus ulcer	0.02 < P < 0.05	n.s.	0.02	n.s.	0.02 < P < 0.05	n.s.	n.s.	n.s.	n.s.	<0.01
Duodenal ulcer = duodenal + gastric ulcer	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Duodenal > prepyloric ulcer	<0.01	0.01 < F < 0.05	<0.01	<0.001	<0.001	<0.001	<0.001	<0.001	n.s.	0.02 < P < 0.05
Acute = chronic duodenal ulcer	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
Proportion of Values above Upper Limit of normal										
Control < duodenal ulcer	n.s.	n.s.	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	n.s.	n.s.
Control = gastric ulcer	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

The probability values in the upper part of the table summarizes the results of the Mann-Whitney tests. The lower part of the table indicates the results of the chi-squared test applied to the proportion of patients with peptic ulcer with secretory response greater than the upper limit of normal. 'P' is considered not significant if greater than 0.05. The direction of the difference between the respective groups is shown in the left hand column.

(Table V). Our low values for basal output were due to low acid concentration of the basal aspirate, not only in the control group (four anacid), but also among the patients with duodenal ulcer (13 anacid). While anacidity of basal secretion had been noted previously in both normal subjects (Kirsner and Ford, 1955) and patients with duodenal ulcer (Littman, 1962; Baron, 1963b; Orr, 1964), its occurrence in patients with duodenal ulcer had been denied (Bruce, Card, Marks, and Sircus, 1959; Grossman *et al.*, 1963), or attributed to the presence of an acute complication such as recent bleeding (Chandler and Watkinson, 1959), or found to follow severe and protracted episodes of the disease (Littman, 1962). The latter two criteria accounted for just over half of our patients with duodenal ulcer with anacid basal juice. Basal acidity bore no relationship to the volume of juice aspirated during the basal hour in any of the groups of patients.

In this study, basal output of gastric juice from patients with duodenal ulcer did not differ in range or distribution from the controls, quite unlike the basal hypersecretion noted in patients with duodenal ulcer in many previous reports. The basal secretion of our patients with gastric ulcer was significantly less than control values, contrary to earlier reports of normal basal acid output in such patients (Table V).

Weak, but statistically significant correlation was noted between the basal and peak stimulated output of acid in all groups of patients and at all levels of acid output (Fig. 5 and Table IX), as noted previously by Hunt and Kay (1954), Kirsner and Ford (1955), and Marks (1961). Moreover, our results confirm that patients with greater response to stimulation

tend to secrete larger volumes of basal juice than patients whose response to histalog is less (Table X). Unlike Sircus (1960) and Baron (1963b), but like Hunt and Kay (1954), we found that the ratio of basal to peak acid output was similar in control subjects and in patients with duodenal ulcer (Table XI). Further, the ratio of basal to peak acid output

FIG. 5. Relationship of stimulated to basal secretion in controls and patients with duodenal ulcer, showing low values of peak 30-minute output in some patients with low basal output and tendency of peak 30-minute output to be more uniformly high as basal output increases.

TABLE IX

CORRELATION BETWEEN SOME OF THE PARAMETERS
OF GASTRIC SECRETION

Peak 30-minute output: basal output

Controls	$r = 0.47$	$b^1 = 4.3$	$P < 0.01$
Duodenal ulcer	$r = 0.38$	$b^1 = 3.8$	$P < 0.01$

Peak 30-minute volume: basal volume

Controls	$r = 0.39$	$b^1 = 1.9$	$P < 0.01$
Duodenal ulcer	$r = 0.33$	$b^1 = 1.4$	$P < 0.01$

One and three quarter-hour volume: mean concentration

Controls	$r = 0.26$	$b^1 = 5.8$	$P < 0.01$
Duodenal ulcer	$r = 0.39$	$b^1 = 10.5$	$P < 0.01$

 r = correlation coefficient b^1 = regression coefficient (Bartlett, 1949)

rose as the response to histalog increased (Table XII) but the increase in our patients was not significant, a conclusion similar to that reached by Hunt, Kay, Card, and Sircus (1963), who had calculated that the percentage of the 'maximal' capacity occupied by basal secretion was similar at each level of maximal secretion. Sircus (1960) had suggested that an increase in the ratio of basal to stimulated secretion denoted an increased 'drive' or increased responsiveness of the parietal cell mass, but our results implied that the patients with the low ratios and low basal output had the more significant abnormality of function. We found no group with

dissociation between basal and peak acid output, attributable to excessive vagal activity in the basal state (Sircus, 1960; Baron, 1963b; Orr, 1964). Our finding that basal anacidity or hypoacidity is associated with low concentration of acid in stimulated gastric secretion (Table X), in all categories of patients, seems comparable to the report of Ball (1961) that patients with gastric ulcer and nocturnal anacidity secrete little acid on stimulation of the stomach. Mucosal defects such as 'gastritis' may be responsible for this type of abnormally low secretory response (Bock, Richards, and Witts, 1963; Krentz, 1964) resulting perhaps from rapid leakage rather than failure of secretion of hydrogen ions (Davenport, Warner, and Code, 1964).

The present study has shown even more overlap between acid output of the control population and patients with peptic ulcer than previous studies using histamine (Bruce *et al.*, 1959; Grossman, 1960; Marks, 1961; Baron, 1963a; Marks, Bank, Moshal, and Louw, 1963) or submaximal doses of histalog (Grossman *et al.*, 1963). The hypersecretors with duodenal or gastric ulcer produced an excessive volume of gastric juice, with concentration not different from normal, presumably by means of an increased parietal cell mass (Card and Marks, 1960), while patients of all groups with impaired secretory

TABLE X

MEAN VALUES OF BASAL SECRETION RELATED TO MAGNITUDE OF PEAK SECRETION

	Controls	Duodenal Ulcer	Duodenal + Gastric Ulcer	Prepyloric Ulcer	Corpus Ulcer
<i>Peak 30-min. output (mEq.)</i>	<i>Mean basal output (mEq./hour)</i>				
<10	0.5	0.5	—	0.3	0.6
10-19	1.3	1.3	1.2	0.9	1.3
20-29	2.9	2.4	2.5	1.8	3.4
≥30	—	3.9	3.1	4.5	3.6
<i>Peak 30-min. volume (ml.)</i>	<i>Mean basal volume (ml./hour)</i>				
<100	58	43	14	33	25
100-199	64	66	61	44	64
200-299	91	79	62	81	64
≥300	—	134	84	—	90
<i>Mean concentration (mEq./l.)</i>	<i>Mean basal concentration (mEq./l.)</i>				
<100	17	11	—	13	11
>120	44	40	—	29	24

TABLE XI

MEAN RATIOS OF SECRETORY INDICES¹

	Controls	Duodenal Ulcer	Duodenal + Gastric Ulcer	Prepyloric Ulcer	Corpus Ulcer
<i>Output</i>					
Basal/peak 30 min.	0.10	0.10	0.08	0.08	0.12
Peak 60 min./peak 30 min.	1.82	1.84	1.79	1.79	1.79
One and three-quarter-hour/peak 30 min.	2.82	2.85	2.80	2.75	2.76
<i>Volume</i>					
Basal/peak 30 min.	0.40	0.37	0.38	0.35	0.38
Peak 60 min./peak 30 min.	1.88	1.86	1.83	1.79	1.81
One and three-quarter-hour/peak 30 min.	3.02	2.91	2.86	2.85	2.84

¹The figures denote the mean ratios of secretory data indicated in the left hand column.

FIG. 6. Relationship between total volume of gastric juice produced during the test and mean concentration of acid, showing that low concentration was associated with low volumes of secretion, although the converse was not necessarily true.

responses produced small volumes of gastric juice, often with low concentration of acid (Fig. 6). Patients with duodenal ulcer with low peak output were unable to sustain secretion of acid for the duration of the test as well as the controls or the remainder of the patients with duodenal ulcer (Table XII) and also tended to secrete basal juice with low acid concentration. The aetiological significance of these findings is not clear, but low acid output in these patients could not be correlated with age, duration of the disease, complications such as haemorrhage or presence of concurrent gastric ulcer. Gastric secretion in patients with coincident duodenal and gastric ulcers did not differ from patients with simple duodenal ulcer, as

TABLE XII

Peak 30-minute Output (mEq.)	MEAN RATIOS OF BASAL OUTPUT TO PEAK 30-MIN. OUTPUT RELATED TO MAGNITUDE OF PEAK SECRETION	
	Mean Ratios	
	Controls	Duodenal Ulcer
< 10	0.07 ¹	0.07 ²
10-19	0.10	0.08
20-29	0.12	0.10
≥ 30	—	0.13

¹Three of eight patients had basal anacidity.

²Eight of 12 patients had basal anacidity.

noted previously by Marks and Shay (1959) and Grossman (1960), although other reports (Ball, 1961; Baron, 1963a) had noted that secretion was less in patients with combined ulcers. As in previous reports (Hunt and Kay, 1954; Baron, 1963a; Grossman *et al.*, 1963), we found no correlation between the acid output and length of clinical history of the duodenal ulcer, but we were able to show that patients whose duodenal ulcer was a serious clinical problem, especially if sufficient to require surgery, had a significantly higher mean rate of acid secretion than patients whose duodenal ulcer was clinically less troublesome. Our results indicate that measurement of gastric acid secretion may help in assessing the prognosis of ulcer disease, but a prospective study will be necessary for confirmation.

In this investigation, patients with prepyloric ulcer showed secretory patterns similar to the controls, as noted previously by Marks and Shay (1959), thus differing from both patients with duodenal ulcer and ulcer of the remainder of the stomach. The functional differences between the two types of gastric ulcer suggest the presence of more severe degrees of gastric mucosal abnormality in patients with corpus ulcers.

Most of the patients with ulcer of the body of the stomach produced less gastric juice, both during the basal period and after stimulation, than did the controls. Moreover, the gastric aspirate from these patients contained very significantly lower concentrations of acid. Nevertheless, some of the patients with corpus ulcer showed no evidence of secretory impairment and actually produced more acid than normal. These patients were not clinically different from those with impaired secretion and coincident duodenal ulcer was excluded at operation. The sharp separation, without overlap, of these types of secretory pattern in patients with corpus ulcer suggests that this group is not aetiological homogeneous. Marks and Shay (1959) had shown a similar range of secretion in patients with gastric ulcer, although they did not describe such sharp separation as in our series, perhaps due to differences in technique or vagaries in the selection of patients.

Histalog, in the dose used in this study, was found to be a very satisfactory gastric secretory stimulant. Side effects were not noted, apart from a sensation of warmth accompanied by flushing. Secretion was well sustained, higher than in any previous report and repeatability was excellent. The peak 30-minute response was used for most of the comparisons and calculations in this investigation, since separation of the different categories of patients was not improved by use of peak 60-minute or one-and-three-quarter-hour values (Table XIII).

TABLE XIII

MEAN RATIOS OF ONE AND THREE-QUARTER-HOUR
OUTPUT TO PEAK 30-MINUTE OUTPUT IN PATIENTS WITH
DUODENAL ULCER

	Peak 30-minute Output (mEq.)		
	<10	≥30	P
Mean ratio ¹			
1½ hour/peak 30 min. output	2.72	2.94	<0.01

¹The values of the ratios indicate that patients who secrete more than the upper limit of normal sustain secretion significantly better than patients with a poor response to histalog.

SUMMARY

Histalog, in a dose of 1.5 mg. per kg. body weight, has provided a safe and repeatable means of eliciting maximal gastric stimulation. However, owing to the marked overlap of secretory responses, distinction between different diagnostic categories of patients has been unsatisfactory. Although patients with duodenal ulcer tended to secrete more than control subjects, only one sixth secreted more than the upper limit of normal (30 mEq. in 30 minutes) while 10% of patients of both groups showed a poor response (less than 10 mEq. in 30 minutes). Patients whose duodenal ulcer was a severe clinical problem, especially those requiring surgery, secreted acid at a significantly higher mean level than patients whose ulcer was clinically less troublesome. Patients with gastric ulcer, particularly when situated in the body of the stomach, tended to secrete less acid than the controls, but a few showed the same degree of hypersecretion in patients with duodenal ulcer.

In this study, basal secretion was lower and stimulated secretion greater than in previous reports. Some correlation between basal and stimulated secretion was noted in all groups of patients. Patients whose response to histalog was small and poorly sustained, with low concentration of acid, secreted small volumes of juice during the basal hour, while those with normal or excessive response to histalog tended to secrete well during the basal period.

From our results, we have been unable to define the pathophysiological basis of duodenal ulcer, except to suggest that increased parietal cell mass is unlikely to be the sole, or perhaps even the most important determinant, in many patients. Instead, we have been able to show that impaired secretory capacity, suggesting gastric mucosal damage, is associated with peptic ulcer in a considerable proportion of patients of all categories.

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