GASTRIC ACID SECRETION IN PATIENTS WITH DUODENAL ULCER AND IN A CONTROL GROUP, AS DETERMINED BY THE AUGMENTED HISTAMINE TEST

By Fung Wye Poh, M.B.B.S., M.R.A.C.P.
(Department of Clinical Medicine, University of Singapore)

Histamine was first shown to be a stimulant of gastric secretion in the dog by Popielski (1920); and soon after this effect was demonstrated in man by Carnot et al (1922). The superiority of Histamine over other stimulators of gastric secretion was increasingly appreciated especially in defining achlorhydria, and soon it replaced the conventional fractional test meal in many centres (Polland, 1933). This lead to the introduction of a quantitative test by Ihre 1938).

When Histamine is given in increasing doses the gastric acid output also increases until a stage is reached when larger doses do not evoke any further increase in acid output. This is the maximal acid secretory response, which may bear a definite relationship to the parietal cell mass (the total number of parietal cells in the stomach—(Adam et al 1954). The parietal cell mass may be the determining factor in the amount of acid that can be produced by the stomach—(Guiss, et al 1948; Tongen, 1950; Meyers, 1948; Cox, 1952). With the advent of antihistamine drugs, it was found that parenteral antihistamine drugs antagonise the unpleasant side effects of large doses of Histamine without affecting its stimulant action on gastric secretion. This lead to the determination of gastric acid output in response to graded doses of Histamine given parenterally. Kay (1953) established that the smallest dose of Histamine acid phospate that would produce a maximal acid secretory response was 0·04 mg. per kg. body weight. This forms the basis of the augmented Histamine test, which is now widely accepted as a reliable routine test of gastric acid secretion. Reproducibility of results has been found to be good, and responses have agreed well with that obtained by maximal doses of Histamine given intravenously. The maximal acid output thus produced has also been shown to correlate well with the parietal cell mass in both humans—(Card, et al 1960) and dogs—(Marks, et al 1960). This means that the augmented Histamine test is a good clinical determination of the parietal cell mass. Under maximal Histamine stimulation, about 50 million parietal cells produce 1 meq. of Hcl.per hour in both man and dog—(Marks, 1961).

METHOD

After an overnight fast, an 18F cleland double lumen tube is passed into the stomach. The fasting residue is aspirated and discarded. A basal secretion is then collected for 1 hour by intermittent aspiration at 5 to 10 minute intervals. 100 mg. of mepyramine maleate is injected i.m. 30 minutes after commencement of basal collection. At the end of the basal hour, Histamine acid phosphate (0·04 mg. per kg. body weight) is given by subcutaneous injection. A one hour post-histamine collection is then obtained. The pH of the basal and post-histamine samples are determined by a pH-meter (radiometer), and the acid output determined by direct titration against n/20 NaOH using phenol red as the indicator, and the results expressed as MEQ. HCL. per hour. The basal acid output (BAO) and the maximal acid output (MAO) are thus determined.

RESULTS

The results are shown in Tables I, II, III, IV; and Figures I, II and III.

35 patients with duodenal ulcer, proven radiologically by barium studies, were included in this study. There were 29 males and 6 females in this group. Their ages range from 16 years to 67 years with a mean of 38·1 years. The group was predominently Chinese (28 Chinese, 3 Malays, 3 Indians, and 1 Philippino). All these patients had a history of chronic duodenal ulcer, and are being followed up in the Gastroenterology Clinic of the Department of Clinical Medicine.

The control group consists of 14 patients who have no evidence of peptic ulceration. There were 5 males and 9 females. Their ages range from 12 years to 64 years with a mean of 37·1 years. 13 are Chinese. They were seen for the following complaints: Chest Pain (2 patients), Subacute Dermatitis (1), Neurodermatitis,

TABLE I

	Duodenal Ulcer	Controls
1. No. of patients	35	14
2. Males: females	29:6	5:9
3. Racial distribution:		
Chinese	28	13
Malay	3	0
Indian	3	0
Others	1	1
4. Age — mean range	38.1 years	37.1 years
	16 years—67 years	12 years—64 years.

TABLE II

BASAL ACID OUTPUT IN PATIENTS WITH PROVEN ULCER VERSUS A CONTROL GROUP. (W.P. FUNG, 1967).

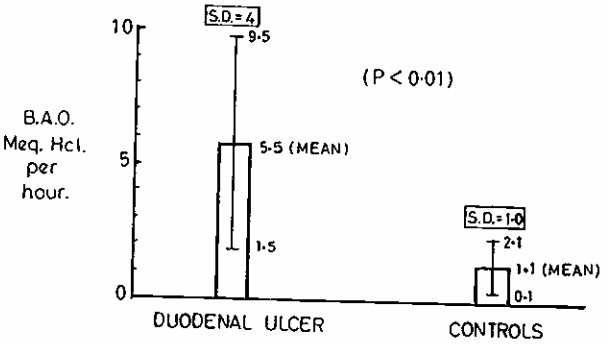

TABLE III

HISTAMINE STIMULATED MAXIMAL ACID OUTPUT IN PATIENTS WITH DUODENAL ULCER VERSUS A CONTROL GROUP. (W.P. FUNG, 1967).

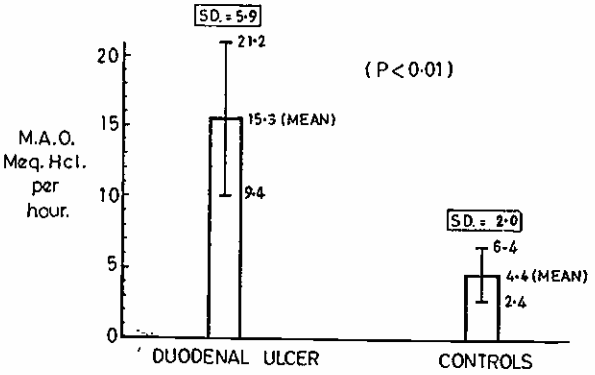

TABLE IV

BASAL AND HISTAMINE-STIMULATED MAXIMAL ACID OUTPUT FROM VARIOUS CENTRES

Centre	Basal Acid Output[1]		Maximal Acid Output[1]		Ratio B.A.O./M.A.O.(%)	
	Control	Duodenal ulcer	Control	Duodenal ulcer	Control	Duodenal ulcer
1. Edinburgh. (Bruce et at. 1959)	2.5	6.0	22.0	37.5	11.1	16.0
2. Glasgow. (Kay. 1953)	2.2	6.8	22.2	37.0	9.9	18.3
3. Philadelphia. (Marks et al. 1961)	2.7	5.4	28.2	39.6	11.6	13.7
4. Delhi. (Goyal et al. 1966)	2.99	5.46	14.48	24.38	20.1	22.4
5. Singapore. (W. P. Fung. 1967)	1.1	5.5	4.4	15.3	25.0	35.9

([1] Mean values expressed in Meq. Hcl per hour)

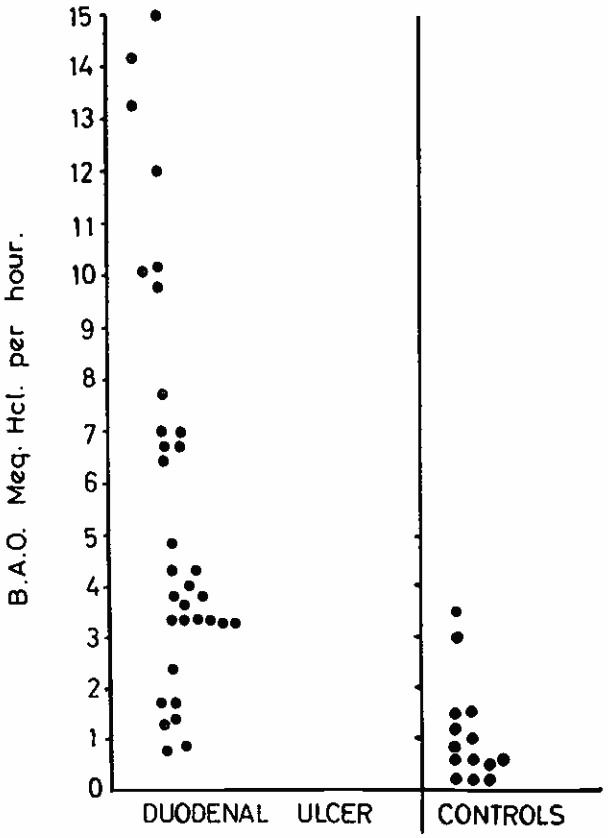

Fig.1. Distribution of B.A.O. in patients with proven duodenal ulcer versus a control group. (W.P. Fung, 1967).

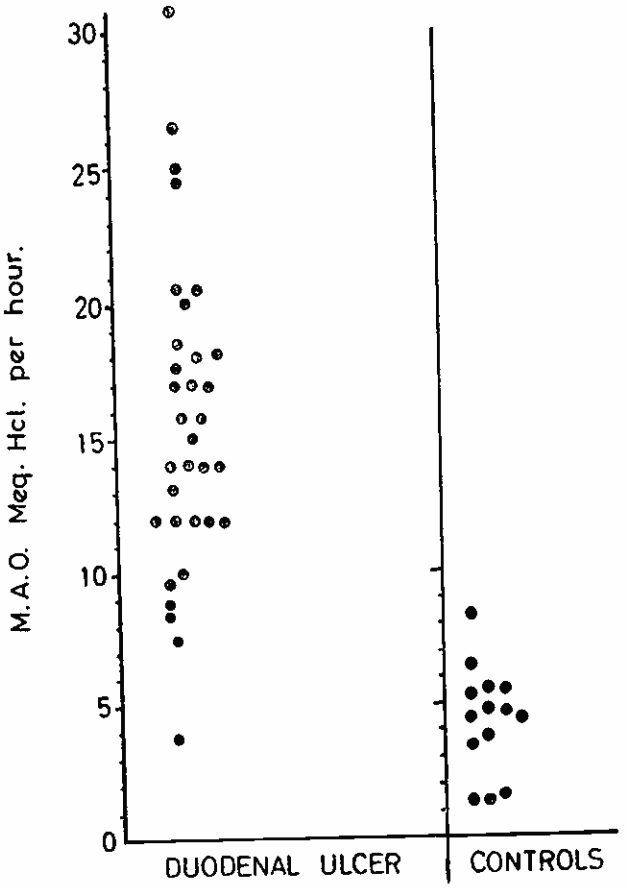

Fig. 2. Distribution of M.A.O. in patients with duodenal ulcer versus a control group. (W.P. Fung, 1967).

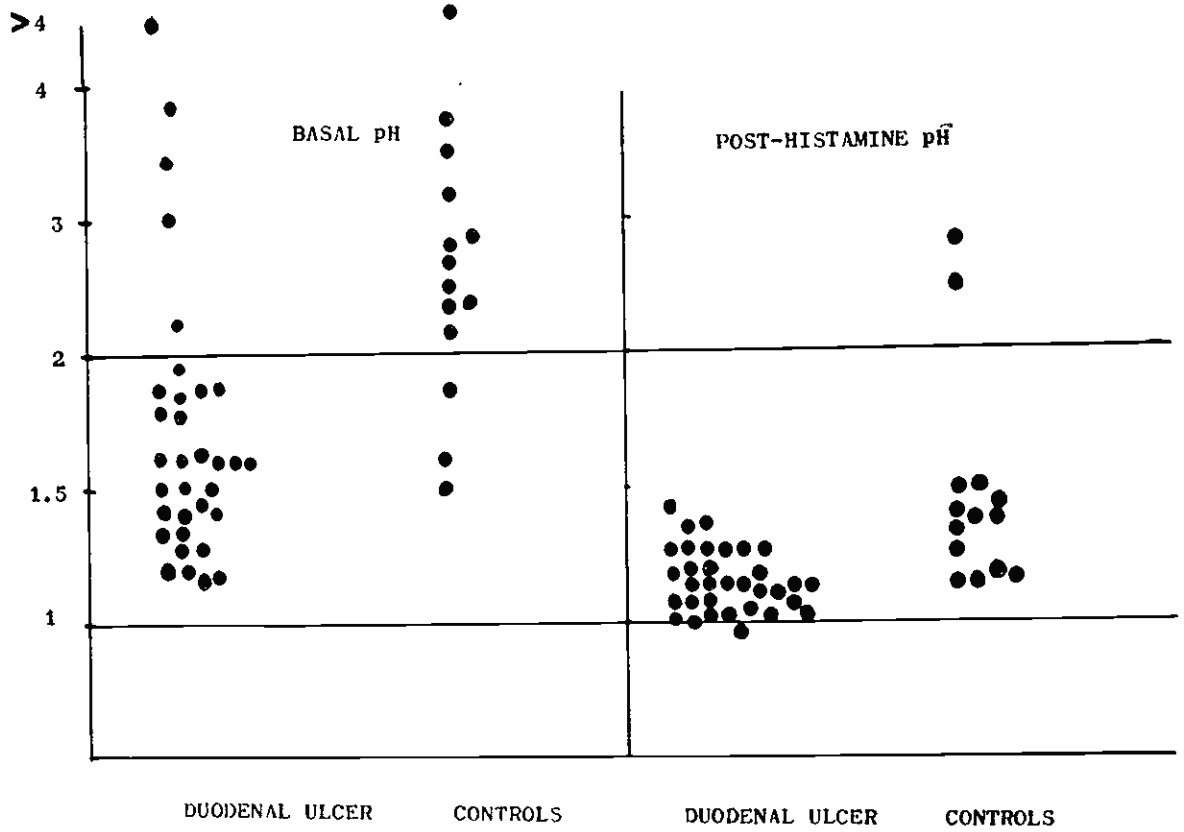

Fig. 3. pH of basal and post-histamine gastric samples in duodenal ulcers versus controls.

(1), Alopecia (1), Acne (1), Psoriasis (1), Vitiligo (2), Ureteric Calculus (1), Pyelonephritis (1) Anxiety Neurosis (1), Diarrhoea (1), and Post-Dengue (1).

The results of the basal and maximal acid outputs in these two groups are shown in Tables II, III, and Figures 1, 2, and 3. These results are compared with those from other centres—(Bruce, et al 1959; Kay, 1953; Marks and Shay, 1961)—in Table IV.

DISCUSSION

The difference between the mean basal acid output (BAO) and the mean maximal acid output (MAO) of the duodenal ulcer group and that of the control group was highly significant ($P < 0{\cdot}01$)—Tables II and III. A BAO above 2·1 MEQ. per hour would be considered abnormal, and if around 5·5 MEQ. per hour or above, would strongly suggest Duodenal Ulceration. A MAO above 6·4 MEQ. per hour would be considered abnormal, and if around 15·3 MEQ. per hour or above, would strongly suggest Duodenal Ulceration.

Figures I and II show that there is a wide variation of both BAO and MAO in Duodenal Ulcer patients, and to a lesser extent in the control group. This is in agreement with other workers—(Gundry, et al 1967; Levin, et al 1951; Grossman, et al 1963 and Wormsley, et al 1965)—and probably indicates multiple genetic factors.

In the Duodenal Ulcer group out of 35 patients 6 had a low BAO and a high MAO; while 28 had a high BAO and a high MAO. It is interesting to note that in the results of Gundry, et al (1967) Basal Achlorhydria was found in 4 patients, and a distinctly low BAO in another 6 of the 40 patients with Duodenal Ulcer. In the present series Achlorhydria was not found, but 6 of the Duodenal Ulcer patients had a low or normal BAO. This indicates that Gastric Hyperacidity maybe due to multiple mechanisms in Duodenal Ulcers. Since the MAO is a good index of the parietal cell mass (PCM) those Duodenal Ulcer patients with a low or normal BAO and a high MAO may represent a group where there is little stimulation of the PCM under basal conditions; whereas those with a high BAO and high MAO would probably indicate increased stimulation of their PCM under basal conditions. Psychogenic factors may be very important in this latter group. Duodenal Ulcer patients could thus be grouped into: (1) those with low or normal BAO and high MAO; and (2) those with high BAO and high MAO.

When comparing the results with that of other centres (Table IV) the mean BAO and MAO of the control group are generally lower than that from Edinburgh, Glasgow, Philadelphia, and Delhi. In the Duodenal Ulcer group the mean BAO in the present series is very similar to that of the others, and almost the same as that from Philadelphia, and Delhi (5·4 to 5·5 MEQ. per hr.).

In the MAO however there is marked difference, both in the control and Duodenal Ulcer groups, between that from the other centres (Edinburgh, Glasgow, and Philadelphia) on the one hand, and that from Delhi and the present series on the other. The latter results are lower than the former. The mean and the highest MAO in the present Duodenal Ulcer series were 15·3 and 31·2 MEQ. per hr. respectively as compared to a mean MAO of 37·5 MEQ. per her from Edinburgh. This would either mean a difference in parietal cell mass or a difference in the capacity of the PCM to secrete acid under maximal Histamine stimulation. That this may represent a racial difference is not unlikely, but no firm conclusion can be drawn.

The ratio BAO/MAO is important in the differentiation between Peptic Ulceration secondary to an Ulcerogenic Tumour of the pancreas and ordinary Peptic Ulceration. It has been stated that in the latter the BAO is seldom more than 35% and never more than 43% of the MAO (Marks, 1961), whereas in the Zollinger-Ellison syndrome the ratio is almost always greater than 60%—(Zollinger and Ellison, 1955; Marks, et al 1961; Grossman, et al 1961). It is interesting to note that because of the lower MAO results the mean BAO/MAO for control and Duodenal Ulcer groups are significantly higher in both the Delhi and the present series, when compared to that from Edinburgh, Glasgow, and Philadelphia. Goyal, et al (1967) found among their 33 Duodenal Ulcer patients, 4 patients who secreted a BAO of more than 43% of the MAO. In the present series 11 out of the 35 Duodenal Ulcer patients had a BAO more than 43% of the MAO, but none has to date any firm evidence to suggest the presence of an Ulcerogenic Tumour of the pancreas. The significance of these differences in gastric secretory patterns between the various racial groups is still not clear, but that these differences exist is beyond doubt.

SUMMARY

The basal and Histamine stimulated maximal acid output were determined in 35 patients

with radiologically proven Duodenal Ulcer, and this was compared with a control group of 14 patients who had no evidence of Peptic Ulceration.

The mean basal acid output was found to be 1·1 MEQ. per hour (standard deviation of 1·0) in the control group, and 5·5 MEQ. per hour (standard deviation of 4·0) in the Duodenal Ulcer group. The difference was highly significant ($P < 0·01$). The mean maximal acid output was found to be 4·4 MEQ. per hour (standard deviation of 2·0) in the control group, and 15·3 MEQ. per hour (standard deviation of 5·9) in the Duodenal Ulcer group. The difference was highly significance ($P < 0·01$).

There was a wide variation in the acid outputs in the Duodenal Ulcer group, and to a lesser extent in the controls.

28 patients with Duodenal Ulcer had a high basal and a high maximal acid output, while 6 Duodenal Ulcer patients had a low or normal basal acid ouput and a high maximal acid output.

The basal and maximal acid outputs in the control group were generally lower than that reported from the western centres. In the Duodenal Ulcer group the basal acid output (mean) was similar to that of the western centres, but the mean maximal acid output was lower. This resulted in a higher BAO/MAO ratio in the present series. This is in agreement with the results from Delhi. The possibility of racial differences to account for this was discussed.

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