

## THE AUGMENTED HISTAMINE TEST\*

## AN ANALYSIS OF 672 CONSECUTIVE TESTS

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Tests of gastric-acid secretion, although first used before the turn of the century, have not yet gained full acceptance as routine procedures in all gastroduodenal disorders. This is due largely to the inexact nature of the tests used in the past, to the diagnostic limitations imposed by the wide range of secretory responses found in patients free of gastroduodenal disease, to the tedium of intubation, and to the relative frequency with which an adequate history coupled with a barium study will permit a diagnosis to be made. The trend in recent years has been toward the development of quantitative tests which, apart from having some diagnostic merit, shed light on the disturbed physiology associated with, or responsible for, various types of gastroduodenal disease, particularly duodenal ulceration.

The magnitude of the acid secretory response of an individual depends largely on the total number of parietal cells (parietal cell mass, PCM) and on the nervous and hormonal stimuli acting on them. Recognition of the possible role of these factors, and in particular the PCM, in the pathogenesis of duodenal ulcers, has emphasized the need for a simple and reliable method of measuring these variables. The augmented histamine test,<sup>1,3</sup> a quantitative test of acid secretion which yields information on basal secretion and the response to maximal histamine stimulation (maximal acid output, MAO), would appear to be the best available method of satisfying this need. The MAO in tests repeated in the same individual has been found to be remarkably constant,<sup>1,2,4</sup> and studies in man<sup>5</sup> and the dog<sup>6</sup> indicate that the MAO provides a reliable measure of the PCM; about 50 million parietal cells produce 1 mEq. of HCl an hour under conditions of maximal histamine stimulation in both man and the dog. Although the MAO is largely dependent on the PCM, available evidence suggests that basal secretion reflects not only the PCM, but also the magnitude of the sum of cholinergic and humoral stimuli acting on the parietal cells.

In the present paper we wish to report on our experience with the augmented histamine test over the past 2 years, and to compare our findings with similar data reported from other centres.

## TECHNIQUE

The technique of the augmented histamine test is simple.<sup>1,3</sup> The fasting patient was intubated with a radio-opaque Levin tube, and its position in the stomach adjusted under fluoroscopic control. With the patient lying comfortably on his back or

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in the left lateral position, the fasting contents were aspirated and basal secretion collected for one hour by continuous suction, supplemented by manual aspiration. An antihistamine, 50 mg. of mepyramine maleate ('neoantergan', 'anthisan'), was given intramuscularly 30 minutes after the commencement of basal collection to minimize the unpleasant side-effects of the histamine acid phosphate (0.04 mg. per kg. body weight) which was administered subcutaneously at the end of the basal hour. The gastric contents were collected in 15-minute samples for a further hour following the injection of histamine.

Aliquots from each of the samples were titrated with N/20 NaOH, using Töpfers reagent and phenolphthalein as indicators for 'free' and 'total' acid concentration, respectively; the 'total' acid output was calculated by multiplying the volume of the gastric juice by the acid concentration, the result being expressed in mEq. The output over the hour following histamine stimulation, the maximal acid output (MAO), was adopted as the measure of the post-histamine response to facilitate comparison of our findings with the data reported from most other centres; the output during the half-hour period from 15-45 minutes after the injection of histamine could have been equally well employed as a measure of the post-histamine response. The pH of the samples was determined electrometrically in tests in which 'free' acid was not present in any of the samples; a fall in pH to below 6 was considered evidence of acid secretion, and the MAO was arbitrarily recorded as 0.1 mEq. in such cases. Absolute achlorhydria was regarded as a failure of the pH to fall below 6 following histamine stimulation; the 'total' acid output was ignored in such cases, and the MAO recorded as 0.

## RESULTS

## Control Subjects

A group of hospital controls consisted of 20 ambulant patients free from gastro-intestinal disorder, admitted for minor surgical procedures. Their ages ranged from 27 to 57 years, and their mean age was 45 years. Basal secretion ranged from 0 to 13.8 mEq./hr., with a mean value of 4.0 mEq./hr. The MAO varied between 4.9 and 38.9 mEq./hr., with a mean value of 21.7 mEq./hr. Comparison of the mean values in the present series with those found in the Philadelphia series<sup>8</sup> suggested that the control subjects in Cape Town and Philadelphia could be treated as a single population. The frequency distribution of basal secretion and MAO in the combined group of male controls is illustrated in Fig. 1.

The present series did not include any female control subjects. Since the Philadelphia data<sup>8</sup> for female controls agreed closely with that reported in other available series,<sup>2,9</sup> it was considered justifiable to use the Philadelphia data as a basis of comparison in the present series. The Philadelphia series comprised 15 female controls ranging in age from 18 to 68 years, with a mean age of 46 years. Basal secretion varied from 0 to 6.5 mEq./hr. and MAO from 0.1 to 29.2 mEq./hr. The mean values were 1.9 and 15.0 mEq./hr. respectively. Their frequency distribution is represented in Fig. 2.

## Students

There were 74 male students, ranging in age from 18 to 27 years. They comprised almost an entire second-year medical class. Several admitted to occasional post-prandial heartburn, and a small number gave a history suggestive of ulcer dyspepsia; barium studies had been carried out in a few of these, but none had radiological evidence of peptic ulceration. Basal secretion varied between 0 and 22.7 mEq./hr., with a mean value of 5.6 mEq./hr., and the MAO ranged from 1.4 to 61.3

mEq./hr., with a mean value of 28.5 mEq./hr. The frequency distribution of the basal secretion and MAO is shown in Fig. 1. Only 1 student failed to secrete 'free' acid under

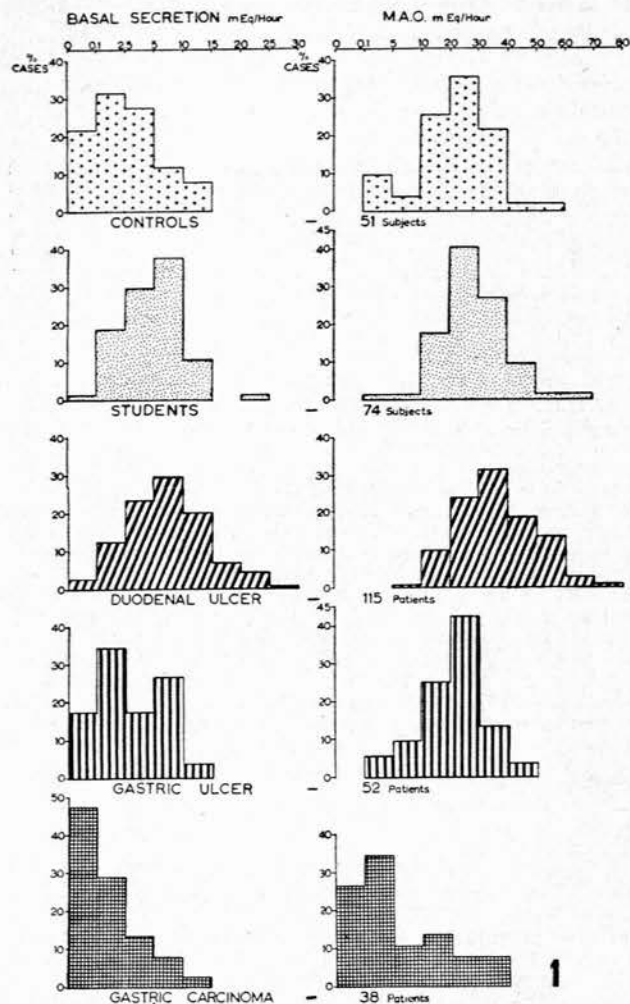


Fig. 1. Frequency distribution of basal secretion and MAO in male control subjects, students, and patients with duodenal ulcer, gastric ulcer, and carcinoma of the stomach.

basal conditions, and not one showed a histamine-fast achlorhydria; indeed only 2 students had an MAO of less than 10 mEq./hr. On the other hand, 13 of the 74 students were clearly hypersecretors; both basal secretion and the MAO exceeded 10 mEq./hr. and 40 mEq./hr. respectively in 5, and the remaining 8 showed either basal hypersecretion (>10 mEq./hr.) or an MAO greater than 40 mEq./hr. The student with an MAO of 61.3 mEq./hr. was troubled by only occasional postprandial heartburn. The MAO tended to be related to body weight in the student group, and it is of interest that all students with an MAO of 40 mEq./hr. weighed more than 170 lb.

#### Duodenal-ulcer Patients

This series included 144 patients with duodenal ulcer, exclusive of those in whom duodenal scarring or ulceration was associated with gastric ulcer. The group comprised 115 males, varying between 15 and 83 years of age, and 29 females, ranging from 24 to 77 years of age. The male group comprised 64 European and 51 non-European patients; the latter included 1 Swazi and 3 Bantu males. The female group was

made up of 20 European and 9 non-European patients; there were no Bantu females in this group.

**Males:** The mean basal secretion was 7.9 mEq./hr. (ranging from 0 to 25.5 mEq./hr.,  $SD \pm 5.90$ ), and the mean MAO was 36.7 mEq./hr. (ranging from 9.5 to 75.3 mEq./hr.,  $SD \pm 12.8$ ). There was no significant difference ( $P > 0.2$ ) between the races with regard to both basal secretion and MAO. The mean basal secretion and MAO were almost double the values found in the control group. The mean MAO agreed very closely with that found in other series,<sup>2,4,10</sup> but the mean basal secretion was slightly greater. Fig. 1 shows that basal secretion exceeded 10 mEq./hr. in 32% of patients. The MAO was less than 30 mEq./hr. in 34% of patients.

**Females:** The mean basal secretion was 4.1 mEq./hr. (ranging from 0 to 10.6 mEq./hr.,  $SD \pm 2.41$ ) and the mean MAO was 23.6 mEq./hr. (ranging from 9.3 to 38.1 mEq./hr.,  $SD \pm 7.47$ ). There was again no significant difference ( $P > 0.4$ ) between the races with regard to basal secretion and MAO. The mean values were significantly greater than the respective values in the female control group; they agreed with those reported from Edinburgh,<sup>2</sup> but were lower than those found in the small Philadelphia group.<sup>3</sup>

#### Gastric Ulcer

There were 72 patients in this group, of whom 52 were males and 20 females. Their ages varied between 19 and 70, and 31 and 74 years respectively.

Gastric ulcer was associated with duodenal scarring or ulceration in 9 of the 72 patients. The male group comprised 23 European and 29 non-European patients; 2 of the latter were Bantu males. The female group was made up of 14 European and 6 non-European patients. The only Bantu female with peptic ulceration in the present series was a patient in whom gastric ulceration and duodenal scarring were components of the Zollinger-Ellison syndrome.<sup>11</sup> She was not included in the gastric-ulcer group and will be considered separately.

**Males:** Basal secretion ranged from 0 to 12.4 mEq./hr. (mean 3.6 mEq./hr.,  $SD \pm 3.40$ ), and the MAO varied between 0.1 and 46.5 mEq./hr. (mean 21.3 mEq./hr.,  $SD \pm 9.95$ ). These means were similar to the values found in control subjects, and Fig. 2 shows that the frequency distribution of basal secretion and MAO was also comparable to that found in the control groups. The mean values also agreed closely with those reported in other series. There was no significant difference ( $P > 0.4$ ) between the races with regard to basal secretion or MAO, but it is of interest that the lesion was

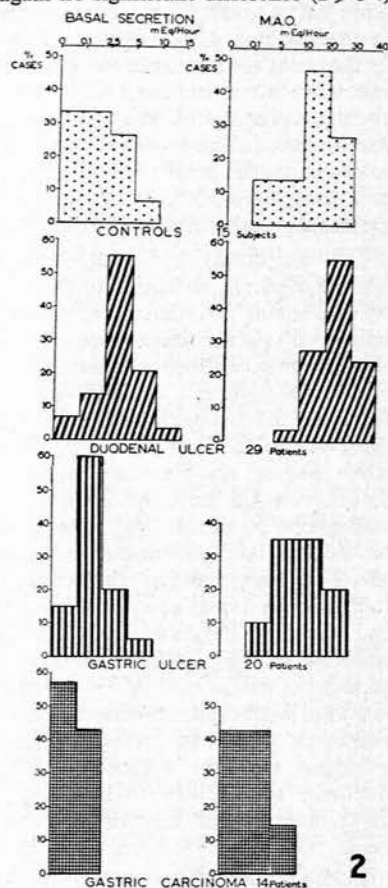


Fig. 2. Frequency distribution of basal secretion and MAO in female control subjects and patients with duodenal ulcer, gastric ulcer, and carcinoma of the stomach.

distal to the incisura angularis in 10 of the 23 European and only 4 of the 29 non-European patients. The patients with antral or pyloric lesions had a mean basal secretion of 5.7 mEq./hr., and a mean MAO of 27.5 mEq./hr.

**Females:** The mean basal secretion was 1.6 mEq./hr. (ranging from 0 to 5.3 mEq./hr., SD  $\pm$  1.39) and the mean MAO 15.8 mEq./hr. (ranging from 3.4 to 27.5 mEq./hr., SD  $\pm$  10.87). The mean values were similar to those found in the control group, and to those reported in other series<sup>2,4</sup> of females with gastric ulcer. The mean values for Europeans were almost identical with those for non-Europeans.

#### Gastric Carcinoma

This group consisted of 52 patients, 38 males and 14 females. Their ages varied between 36 and 77 years in the males, and between 39 and 86 years in the females. Eighteen of the 38 males were European and 20 non-European; the latter included 2 Bantu patients. The female group comprised 7 Europeans and 7 non-Europeans; there were again no Bantu females.

**Males:** The mean basal secretion was 1.7 mEq./hr. (ranging from 0 to 13.6 mEq./hr., SD  $\pm$  3.04) and the mean MAO 8.0 mEq./hr. (ranging from 0 to 38.3 mEq./hr., SD  $\pm$  11.57). Acid secretion was significantly lower ( $P < .001$ ) than that found in control or gastric-ulcer subjects, but Fig. 1 shows the extent of the overlap between the groups. The MAO exceeded 10 mEq./hr. in 29% of male patients with gastric cancer, and was greater than 20 mEq./hr. in just under half of these. Histological evidence of malignancy developing on the basis of chronic peptic ulceration was present in 2 of the hypersecretors, one with a mid lesser-curve ulcer and an MAO of 38.3 mEq./hr., and the other with an antral ulcer and an MAO of 34.3 mEq./hr. Absolute achlorhydria was present in 26% of the male patients. There was no significant difference ( $P > 0.1$ ) between Europeans and non-Europeans with regard to both basal secretion and MAO.

**Females:** Basal secretion ranged from 0 to 1.5 mEq./hr., with a mean value of 0.3 mEq./hr., and the MAO varied between 0 and 6.4 mEq./hr., with a mean value of 1.9 mEq./hr. The high incidence of achlorhydria in this group is illustrated in Fig. 2; 57% had basal achlorhydria, and no fewer than 43% showed a histamine-fast achlorhydria.

**Comparison with antral gastric-ulcer findings.** The lesion was distal to the angulus in 21 of the 38 males and in 8 of the 14 females. An antral or pyloric carcinoma was thus present in 56% of the entire group. The mean MAO of the antral and pyloric carcinomas was 8.4 mEq./hr. in males and 3.1 mEq./hr. in females. A comparison between the MAO in patients with antral and pyloric cancer and in patients with benign gastric ulcer in the same area is shown in Fig. 3. There was a highly significant difference between the 2 groups

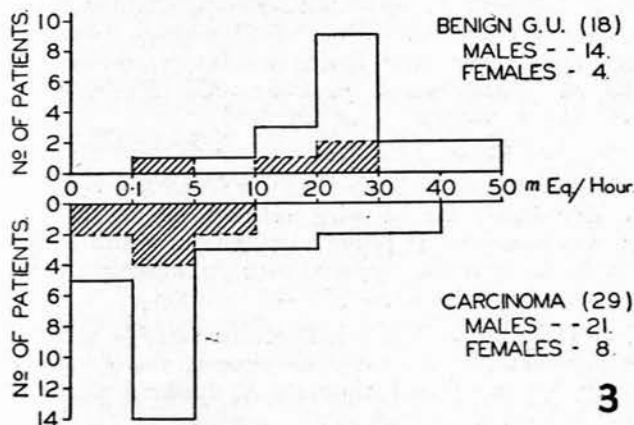


Fig. 3. Comparison of MAO in patients with benign ulcers distal to the angulus with that in patients with carcinoma distal to the angulus. Females are indicated by crosshatched areas.

(males  $P < .001$ , females  $P < .01$ ), but a wide overlap was clearly evident; 72% of patients with benign ulceration had an MAO greater than 20 mEq./hr., whereas 86% of patients

with cancer had an MAO of less than 20 mEq./hr. Achlorhydria, however, was present in 17% of the antral-cancer group, but was not encountered in the peptic-ulcer group.

#### Zollinger-Ellison Syndrome

The series included a Bantu woman with peptic ulceration associated with a non-beta islet-cell tumour of the pancreas.<sup>11</sup> This patient, who presented with 2 gastric ulcers and duodenal scarring, had a basal secretion of 20.7 mEq./hr. and an MAO of 33.7 mEq./hr. Basal hypersecretion was attributed to the gastrin-like substance present in the primary tumour and in the metastases.<sup>12</sup> The high level of basal secretion was 61% of the MAO, a ratio greater than that found in other hypersecretors without the syndrome.

#### Miscellaneous Group

This group consisted of 288 patients, and could be divided into 3 sub-groups:

1. Subsequent investigation failed to reveal any evidence of gastric cancer or pernicious anaemia in 211 patients investigated for dyspepsia, weight loss or anaemia. The group consisted of 118 males and 93 females. Basal secretion in the male patients ranged from 0 to 18.1 mEq./hr., and the MAO from 0 to 49.7 mEq./hr.; the MAO exceeded 40 mEq./hr. in 3 patients, all of whom had hiatus hernia with reflux oesophagitis. Basal secretion in the female patients ranged from 0 to 7.4 mEq./hr., and the MAO from 0 to 29.8 mEq./hr. No fewer than 27 patients, 9 male and 18 female, had a histamine-fast achlorhydria unassociated with pernicious anaemia or gastric carcinoma; the majority of these patients were investigated for dyspepsia, and the remainder all admitted to varying degrees of indigestion.

2. A clinical diagnosis of pernicious anaemia was supported by the finding of histamine-fast achlorhydria in 17 patients. A presumptive diagnosis of pernicious anaemia was refuted by an acid secretory response in a further 10 patients, who are included in the 211 patients in sub-group 1 of this section.

3. Gastrojejunal disease could not be established in 60 postgastrojejunectomy subjects investigated for dyspepsia, 'dumping' symptoms, bleeding or diarrhoea. The highest MAO in the group was 11.6 mEq./hr. The 12 patients with diarrhoea or steatorrhoea were of interest in that all had basal achlorhydria; the MAO ranged from 0 to 3.0 mEq./hr. By contrast, 5 of the 11 patients investigated for bleeding secreted acid under basal conditions; the MAO in these ranged from 0 to 10.8 mEq./hr., with a mean value of 2.8 mEq./hr.

#### Postoperative Dyspepsias

The group included 9 patients with postgastrojejunectomy jejunal ulceration, 7 patients with postgastrojejunectomy gastric or suture-line ulcers and 2 male patients with postgastroenterostomy jejunal ulcers; 1 of the latter 2 was a Bantu male (Fig. 4).

**Jejunal ulceration:** The postgastrojejunectomy group included 6 males and 3 females. The mean basal secretion in the males was 8.3 mEq./hr. (ranging from 3.6 to 13.5 mEq./hr.) and the mean MAO was 27.2 mEq./hr. (ranging from 18.9 to 36.1 mEq./hr.). The female subjects had a mean basal secretion of 6.4 mEq./hr. (ranging from 3.2 to 8.7 mEq./hr.) and a mean MAO of 17.8 mEq./hr. (ranging from 12.6 to 23.8 mEq./hr.). The mean basal secretion was thus appreciably greater, and the mean MAO only slightly lower, than the respective values found in duodenal-ulcer patients with an intact stomach. Basal secretion was also high in the 2 patients with jejunal ulcer following gastroenterostomy (9.2 and 10.2 mEq./hr.); the MAO in these patients was 37.3 and 29.8 mEq./hr.

**Recurrent gastric or suture-line ulceration:** The mean MAO in 7 patients with gastric or suture-line ulceration following gastrojejunectomy was 1.8 mEq./hr. (ranging from 0 to 3.4 mEq./hr.). Only 1 of the patients showed achlorhydria, and it is of interest that the ulcer in her case extended from the gastric on to the jejunal side of the stoma. The ulcers were confined to gastric mucosa in the remaining 6 patients, 1 of whom was a female.

**Stomal obstruction.** Three postgastrojejunectomy subjects with stomal obstruction due to mechanical factors (vagotomy had not been carried out and the obstruction was not due to recurrent ulceration) were investigated. Gastric retention was marked in all 3, but the MAO ranged from 0.3 to 4.0 mEq./hr.

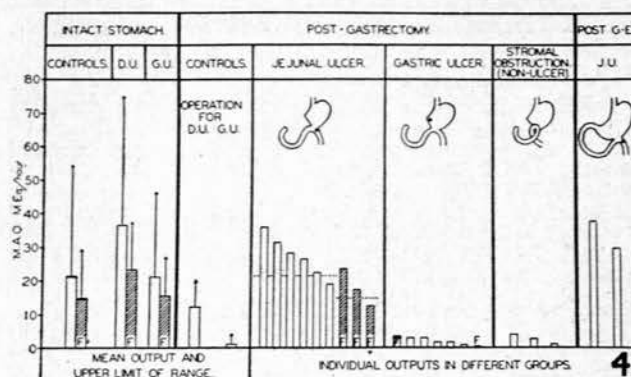


Fig. 4. Application of the augmented histamine test to the problem of postgastroectomy or postgastroenterostomy (post G-E) dyspepsias. D.U. = duodenal ulcer; G.U. = gastric ulcer; J.U. = jejunal ulcer. + = patient who developed a recurrent duodenal ulcer following a Billroth I gastrectomy, but who has been included in the jejunal-ulcer group for convenience. Results in female patients are indicated by F and cross-hatched areas. The mean output in postgastroectomy controls is probably an overestimate, since it was calculated from results obtained by means of stomal blockage<sup>19</sup> in the immediate postoperative period.

Transient gastric retention was frequently observed in patients following vagotomy combined with gastroenterostomy, pyloroplasty or even partial gastrectomy. Basal secretion and MAO were characteristically reduced, but were found to be unusually high in 3 patients; this interesting finding will be considered in a separate paper.

#### Ratio of Basal Secretion to MAO

The ratio of basal secretion to MAO varied between 2 and 40% in all normal or hypersecretors with basal secretion less than 10 mEq./hr. Apart from the patient with the Zollinger-Ellison syndrome, basal secretion exceeded 10 mEq./hr. in 59 patients. The ratio did not exceed 40% in 46, was less than 45% in 54, and less than 50% in 56 of the 59 patients. The ratio exceeded 50% in 3 patients, 1 with a large carcinoma of the antrum (51%), and 2 with 'pyloric stenosis' due to duodenal ulceration (56 and 59%). There was no evidence of a pancreatic tumour in either of these 2 patients, but the possibility of a Zollinger-Ellison syndrome could not be excluded with certainty because of the short follow-up period; pancreatic biopsies were not taken.

#### DISCUSSION

The results of the augmented histamine test carried out in the control and various disease groups were found to agree closely with those reported from other centres.<sup>2,3,9,9</sup> The mean MAO in duodenal-ulcer subjects was almost twice that in controls, whereas the mean value in gastric-ulcer patients was similar to that found in controls; patients with carcinoma of the stomach secreted significantly less acid than controls. As in other series, a wide overlap was found between the various disease groups and between these groups and the controls. Females tended to secrete less acid than males in all groups.

The control and disease groups contained an approximately equal number of European and non-European patients, and there was no significant difference in acid secretion between the two racial groups. Our findings in the males with gastric ulceration, however, suggested a possible difference between the groups with regard to the localization of the lesion in the stomach; the lesion was distal to the angulus in 43% of the Europeans but in only 14% of the non-Europeans. The incidence of gastro-duodenal disease in Bantu males was distinctly low, and in Bantu females virtually nil. Bantu males, all of whom

were urbanized, constituted 4% of the duodenal-ulcer, gastric-ulcer and gastric-carcinoma groups. The series included only one rural Bantu male in whom jejunal ulceration had developed following simple gastroenterostomy carried out for vague abdominal pain. The only Bantu female in the series was a patient in whom gastric ulcers and duodenal scarring were a component of the Zollinger-Ellison syndrome.

The extreme rarity of hyposecretion and absence of histamine-fast achlorhydria in the student group was in keeping with Ihre's findings<sup>13</sup> in a young adult group. The 4% incidence of achlorhydria in Ryle's<sup>14</sup> student group would appear to be excessively high and may well have been due to unsatisfactory positioning of the tube in the stomach and to the weaker stimulant effect of the gruel stimulus employed. The control groups included 7 patients with marked hyposecretion, 5 of whom were more than 60 years of age. The tendency for acid secretion to diminish with increasing age has been noted with other tests of gastric secretion.<sup>15</sup> It may be inferred that this is due to progressive gastritis, which is sufficiently common in health to be regarded as part of the ageing process. However, atrophic gastritis sufficiently extensive to cause histamine-fast achlorhydria was usually associated with mild digestive symptoms; in addition, it is generally accepted that such change carries with it an increased risk of gastric cancer<sup>16</sup> and pernicious anaemia.<sup>17</sup> It is of interest that the control groups did not include a single patient with a histamine-fast achlorhydria, and that varying degrees of dyspepsia were present in all 27 achlorhydric patients free of pernicious anaemia or gastric cancer included in the present series.

The higher incidence of hypersecretion in students than in controls was also of interest. Body weight could hardly be held responsible for the difference since the mean body weight was similar in the two groups, but the student group probably included a number of individuals destined to develop, but as yet showing no overt evidence of, duodenal ulceration. Doll *et al.*,<sup>18</sup> in a follow-up of 100 medical students who had a histamine-augmented fractional test meal, found that 10 out of 85 subjects traced had developed peptic ulcer during the interim period, and that all 10 had been in the group which showed hypersecretion in response to the test meal.

#### Diagnostic Value of the Test

The augmented histamine test was found to be of diagnostic value in the following instances, despite the wide range of secretory responses varying from virtual achlorhydria to moderate hypersecretion in subjects free of gastroduodenal disease:

1. The finding of an MAO greater than 40 mEq./hr. in a patient with an ulcer-type dyspepsia was of value in suggesting the correct diagnosis of duodenal ulceration where initial X-ray studies were negative.

2. The test was especially important in the elucidation of postgastroectomy or postgastroenterostomy dyspepsia or haemorrhage.<sup>19,20</sup> A postgastroectomy MAO greater than 15 mEq./hr. was considered to be strongly suggestive, and an MAO greater than 20 mEq./hr. virtually pathognomonic,

of jejunal ulceration in such patients. Conversely, a very low acid output was considered adequate grounds for virtually excluding a jejunal, but not a gastric, stitch or suture-line ulcer. The value of the test was enhanced by the fact that X-ray studies and gastroscopy in this group of subjects were frequently less reliable than in patients with an intact stomach.

3. The test was the most reliable and indeed the only method of establishing the presence of true achlorhydria,<sup>7</sup> regarded as the failure of the pH to fall below 6 following maximal histamine stimulation; this is traditionally associated with pernicious anaemia or carcinoma of the stomach, but may occur as an isolated finding in patients with an X-ray negative dyspepsia.

4. The test is of some value in the diagnosis of carcinoma of the stomach. Marked hyposecretion or achlorhydria in a subject with a recent story of dyspepsia points to a possible diagnosis of carcinoma of the stomach and the finding of achlorhydria in a patient with radiological evidence of gastric ulceration is virtually pathognomonic of a malignant rather than a benign lesion. An antral or pyloric lesion associated with marked hyposecretion is strongly suggestive of malignancy. The claim<sup>21</sup> that an MAO greater than 20 mEq./hr. 'can be taken almost to exclude carcinoma' has not been substantiated by more recently available data on the subject; no fewer than 16% of our carcinoma patients had an MAO greater than 20 mEq./hr., a figure which agrees well with the 12% figure given by Sircus.<sup>22</sup> The chances of benignity are certainly higher if the MAO is greater than 20 mEq./hr., but the finding of normal or hypersecretion should never be taken to exclude malignancy in any individual patient. The difficulty in differentiation is complicated by the fact that the radiological, gastroscopic and even operative appearance of a malignant lesion may suggest benignity, and that gastric exfoliative cytology may not necessarily be positive.

5. Consideration of the ratio of basal secretion to MAO proved helpful in the pre-operative differentiation of peptic ulceration secondary to an ulcerogenic tumour of the pancreas (Zollinger-Ellison syndrome) from ordinary peptic ulceration.<sup>11</sup> The ratio in patients with the Zollinger-Ellison syndrome is almost always greater than 60%, whereas the ratio in ordinary peptic ulceration is usually less than 40% and very seldom greater than 50%. Gastric retention was present in all 3 patients with a ratio greater than 50%, and it is interesting to speculate whether excessive gastrin release from chronic antral stimulation could not have been responsible for the high ratio in these patients. Whatever the explanation, the finding of a ratio greater than 50% would appear to justify careful search for a pancreatic tumour and, if possible, pancreatic biopsy to exclude diffuse hyperplasia of the islets with an increased ratio of non-beta to beta-cells.

#### *Guide to Operation for Duodenal Ulceration*

Apart from its value in diagnosis, the test offers an important guide to the nature and extent of operation in the surgical management of patients with duodenal ulceration. One of the main objects of surgery is the reduction of acid secretion to a level at which recurrent ulceration is unlikely. Although the majority of patients with duodenal

ulcer had an MAO ranging between 20 and 40 mEq./hr., the MAO in 11% of them varied from 9.5 to 20 mEq./hr. and in 35% from 40.1 to as much as 75.3 mEq./hr. Acid secretion in patients with postgastrectomy jejunal ulceration has been found, in this and in other series, to be of the order found in the average duodenal-ulcer subject before operation, and there is little doubt that this high level of secretion is due to insufficient resection of the acid-bearing area of the stomach with very high pre-operative acid secretion.<sup>20</sup> Such patients require a procedure more extensive than a standard gastrectomy to reduce acid secretion to a level at which subsequent ulceration is unlikely, and in them the combination of vagotomy and standard gastrectomy appears to be the operation of choice.

#### CONCLUSION

The augmented histamine test, gastroscopy and gastric exfoliative cytology constitute an important triad which may add considerably to the information gained by clinical and radiological examination. The finding of marked hyposecretion or achlorhydria in a patient with an X-ray-negative dyspepsia makes gastroscopy, exfoliative cytology and even repeat barium studies mandatory, whereas the finding of an MAO greater than 40 mEq./hr. suggests a diagnosis of duodenal ulcer. Gastroscopy\* and exfoliative cytology\*\* have already been shown to be of great value in the diagnosis of both chronic ulcer and carcinoma of the stomach in patients with a low or normal level of secretion. This battery of investigations is thus of great help in reducing the likelihood of missing a diagnosis of peptic ulceration or carcinoma, a problem which is particularly important in hospital clinics handling country patients referred from as far afield as 800 miles.

#### SUMMARY

The augmented histamine test is a simple quantitative test of acid secretion which measures both basal secretion and the response to maximal histamine stimulation — maximal acid output (MAO). The MAO provides an index of the parietal cell mass.

The results of 672 tests carried out in control subjects, male students, and patients with duodenal ulcer, gastric ulcer, carcinoma of the stomach, jejunal ulcer, gastric-remnant ulceration, and other miscellaneous dyspepsias, are presented. The mean basal secretion and MAO in duodenal subjects were significantly greater than the mean values in controls, which in turn were significantly greater than the mean values in patients with carcinoma of the stomach. A wide overlap was found between the various groups, however. The augmented histamine test, like other tests of gastric secretion, thus yielded information that was supportive rather than diagnostic, and suggestive rather than pathognomonic.

Despite these limitations, the test was of great value in the elucidation of postgastrectomy dyspepsias, in establishing a diagnosis of true achlorhydria, in helping to distinguish some cases of malignant from benign gastric ulceration, and in supporting a clinical story of duodenal

\* See article by Dr. S. Bank and co-workers on page 812 of this issue of the *Journal*.

\*\* See article by Dr. C. E. Watson on page 816 of this issue of the *Journal*.

ulceration in a few such patients with negative barium studies. Consideration of the ratio of basal secretion to MAO helped to establish the diagnosis of Zollinger-Ellison syndrome in the only Bantu female with peptic ulceration in the series.

The value of the test as a guide to the extent of surgery to be undertaken in patients with duodenal ulcer is discussed.

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