

## ORIGINAL ARTICLE

# Gastric histology, serological markers and age as predictors of gastric acid secretion in patients infected with *Helicobacter pylori*

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**Background:** Acid secretion is intimately associated with most upper gastrointestinal diseases. *Helicobacter pylori* infection is a major environmental factor modifying acid secretion.

**Aim:** To study the association between the pattern of *H pylori* gastritis and gastric secretory function in a large number of subjects without specific upper gastrointestinal disease.

**Methods and materials:** Maximal acid output (MAO) was measured in 255 patients with dyspepsia showing normal endoscopy. Activity and severity of gastritis, atrophy and *H pylori* infection were assessed in body and antral biopsies. The correlations of histological parameters as well as age, sex, height, weight, smoking, serum gastrin, pepsinogen I and II, and their ratio with MAO were determined. Multiple linear regression was used to show the best possible predictors of MAO.

**Results:** Negative relationships: Body atrophy and body-combined (active and chronic) inflammatory scores showed a potent inverse correlation with MAO (correlation coefficients (CC) 0.59 and 0.50, respectively). Body:antral chronic gastritis ratio and body:antral combined inflammation ratio (both with CC=0.49) and age (CC=0.44) were also inversely correlated with MAO. Intestinal metaplasia at both antral and body sites had negative relationships with acid output with CC=0.23 and 0.20, respectively. Positive relationships: Serum pepsinogen I, body *H pylori* density:combined inflammation ratio and pepsinogen I:II ratio with CC of 0.38, 0.38 and 0.30, respectively, correlated with MAO. The *H pylori* density: combined inflammation of both antrum and body positively correlated with MAO (CC=0.29 and 0.38, respectively). Male sex and patient height also positively correlated with acid output. Modelling showed that body combined inflammatory score, body atrophy, age and serum pepsinogen I are independent predictors of acid output ( $R^2=0.62$ ).

**Conclusion:** Combination of body gastritis, body atrophy, age and serum pepsinogen I can be used as predictors of acid-secretory state in populations infected with *H pylori*.

A close association is found between the level of gastric acid secretion and the type of disease affecting the upper gastrointestinal tract. Duodenal ulceration occurs in patients with high acid secretion,<sup>1–5</sup> gastro-oesophageal reflux disease and its complications in patients with normal<sup>6</sup> or high levels of acid secretion,<sup>7–9</sup> gastric ulceration in patients with moderately reduced secretion<sup>10</sup> and gastric cancer in patients with profoundly reduced or absent acid secretion.<sup>11–14</sup>

The level of acid secretion is thought to have a role in the aetiology of these common upper gastrointestinal diseases. Increased gastric acid secretion and duodenal acid load predispose to duodenal ulceration as shown by the Zollinger–Ellison syndrome.<sup>15–16</sup> Absence of gastric acid secretion is thought to predispose to gastric cancer by allowing colonisation of the stomach by carcinogen-synthesising bacteria and also by the reflex hypergastrinaemia stimulating cell proliferation.<sup>17–19</sup> The role of acid in the aetiology of gastro-oesophageal reflux disease is shown by the therapeutic efficacy of acid-inhibitory drugs.

There has been a marked change in the pattern of upper gastrointestinal disease in the Western world over the past century. The incidence of gastric cancer has progressively fallen,<sup>20–22</sup> that of duodenal ulceration has risen and then fallen, and the incidence of reflux disease and its malignant complications has increased.<sup>22–23</sup> These changes in incidence of disease are thought to be partly due to a rise in gastric acid secretion. There are also marked geographical variations in incidence of upper gastrointestinal disease. Reflux disease

and its complications are more common in the Western world versus the Eastern world and the opposite trend is seen for gastric cancer. Again, these variations are believed to be related partly to regional variations in levels of gastric acid secretion.

A major factor known to influence gastric acid secretion is *Helicobacter pylori* infection, which colonises the gastric mucosa of >50% of the world's populations. The effect of the infection on acid secretion is related to the pattern of gastritis, which it induces in the stomach. Previous studies<sup>24–26</sup> have examined acid secretion and *H pylori* gastritis in specific diseases—for example, duodenal ulceration, gastric ulceration and gastric cancer. In patients with duodenal ulcer having antral-predominant gastritis, eradicating *H pylori* lowers serum gastrin, and basal and gastrin-releasing peptides stimulate acid.<sup>27</sup> In patients with low acid secretion due to body-predominant atrophic gastritis, eradicating *H pylori* increases acid secretion.<sup>28</sup> In our study, we examined the relationship between the pattern of *H pylori* gastritis and gastric acid secretion in a large number of patients without specific upper gastrointestinal disease. For various reasons acid secretion is now rarely measured, and we have therefore also assessed the ability to predict the level of acid secretion from gastric histology and serological markers.

**Abbreviations:** ANOVA, analysis of variance; BMI, body mass index; CagA, cytotoxin-associated gene A; CIS, combined inflammatory score; ECL, enterochromaffin-like; IQR, interquartile range; MAO, maximal acid output

## AIM

To assess the value of gastric histology, serological markers and other characteristics as predictors of gastric acid secretion in patients infected with *H pylori*.

## METHODS AND MATERIALS

### Study population

The study included 255 patients with *H pylori*-positive dyspepsia, showing normal upper gastrointestinal endoscopy (ie, no evidence of mucosal ulcerations, erosions or neoplastic changes), who had undergone acid secretory studies in the Gastrointestinal Unit, Gartnavel General Hospital, Glasgow, UK over the past 10 years. Patients who had taken proton pump inhibitor treatment in the past year or H<sub>2</sub> blocker treatment within the previous 3 weeks were not included. Their *H pylori* infection was confirmed by positive results in at least one of two methods, <sup>14</sup>C urea breath test and gastric histology. In all, 123 (48.2%) patients were men and 132 (51.8%) were women. Mean age was 43.4 (SD 13.2) years and range of 18–84 years. Median (interquartile range (IQR)) height, weight and body mass index (BMI (weight (kg)/height<sup>2</sup> (m<sup>2</sup>))) of the patients were 167 (16) cm, 70 (19) kg and 25 (5) kg/m<sup>2</sup>, respectively.

### Histological assessment

Endoscopic biopsies of both the antrum and body region of the stomach were available in 175 patients. The processed biopsy specimens were stained with haematoxylin–eosin and *H pylori*-specific Cresyl fast violet stain. All slides were assessed by a single pathologist for *H pylori* density as well as type and severity of gastritis. The histological criteria applied for evaluation of gastritis were based on the updated Sydney classification of gastritis as follows<sup>29</sup>:

- Gastritis: presence of inflammatory cells of any type in the lamina propria.
- Grade of inflammation: severity of infiltration of lymphocytes and plasma cells.
- Activity of inflammation: Presence of neutrophils in the inflammatory infiltrate. The sum of the grade and activity was expressed as combined inflammatory score (CIS) for each participant with maximum possible score of 6.<sup>30</sup>
- Mucosal atrophy: defined as the separation of the mucosal glands and a decrease in the thickness of mucosa, which is greater in severity than that seen in the inflammation of the lamina propria, and usually associated with an increase in the stromal matrix.
- Intestinal metaplasia: presence of goblet cells with or without other cellular elements of intestinal mucosal and glandular epithelium.

### Acid output measurement

After a 12 h fast, an orogastric tube (Anderson, New York, New York, USA) was swallowed and its position in the dependent part of the stomach was checked using the water recovery test.<sup>31</sup> Intermittent suction was then applied using an intermittent suction unit (Omeda, Columbia, Maryland, USA) that applies suction for 20 s in each 32-s cycle. An intravenous infusion of Pentagastrin (Peptavlon; ICI, Cheshire, UK) was started at a rate of 0.6 µg/kg/h to stimulate maximal acid secretion. Gastric juice was collected for 1 h in 15-min aliquots.

The volume of each 15-minute gastric juice collection was recorded and its hydrogen ion concentration was measured by titration with 0.1 mol/l sodium hydroxide to pH 7 using an autotitrator (Radiometer ETS 822; Copenhagen, Denmark). The acid output per 15-minute period was then calculated by multiplying the volume by the hydrogen ion concentration.

Maximal acid output (MAO) in response to pentagastrin was calculated by taking the mean of two highest consecutive 15-min collections and expressed as mmol/h.

### Serological assay

Blood was drawn from each patient during the visit to the endoscopy unit. Separated serum samples were stored at –70°C until analyses. Serum pepsinogen I and II were assayed with ELISA using monoclonal antibodies to pepsinogen I and II (BIOHIT Diagnostics, Biohit, Devon, UK). Serum gastrin-17 was measured using an ELISA kit from the same supplier. All procedures were carried out according to the manufacturer's instructions and results of pepsinogen I and II reported in µg/l and pmol/l for gastrin-17. The pepsinogen I:II ratio was calculated and reported in fraction. *H pylori* cytotoxin-associated gene A (CagA) antibodies were determined using a polyclonal enzyme immunoassay method, as previously described.<sup>32</sup>

### Statistical analysis

Except for MAO values, all other variables had a relatively non-symmetric distribution; hence a non-parametric test (Spearman's rho) was used for bivariate correlations. All results were presented with a two-sided significance level. A partial correlation analysis with zero orders was used to estimate possible confounders. To test the differences in mean MAO in different levels of gastritis and atrophy, we used one-way analysis of variance (ANOVA) and the retrospective analysis Dunnett test if appropriate. Mann–Whitney U test was used for comparing the age of male and female patients.

Stepwise linear regression was carried out to determine the histological and serological predictors of MAO. Body atrophy score, antral atrophy score, serum pepsinogen I, serum pepsinogen I:II ratio, serum gastrin, age, *H pylori* density of antrum and body, or *H pylori* in one of two sites and body CIS were selected as independent variables and MAO as the dependent variable. Main criteria for probability of F to enter and F to remove of independent variables were ≤0.05 and ≥0.10, respectively. In addition to the standardised coefficients, colinearity statistics were presented for each variable. For most statistical analysis, we used SPSS V.12.0.

## RESULTS

### Acid output and *H pylori*-related gastritis

Density of *H pylori* colonisation in the antral mucosa was positively associated with acid output with a correlation coefficient (CC) of 0.31 (p<0.01), but *H pylori* density of the body did not correlate significantly with the acid secretion (CC = –0.11, p = 0.19). Recalculation of this relationship using a mean score of *H pylori* density at any site showed a positive correlation with acid output (CC = 0.17, p<0.05).

Chronic inflammation of the antrum was positively associated (CC = 0.27, p<0.01) with acid output, although there was a more potent negative association between chronic inflammation of the body mucosa and acid output (CC = –0.41, p<0.01; fig 1). Active inflammation in the antrum did not show any significant relationship with acid output, but in the body it showed a negative correlation (CC = –0.28, p<0.01) with acid output. CISs (ie, active and chronic) of the antrum showed a positive correlation with acid output reaching a peak of 29.3 mmol/h at histological score 4. However, from score 4 to 6 we found a slight decrease in acid output with the lowest value of 24.2 mmol/h at score 6. CIS of the body after a peak of 33.7 mmol/h at score 2 showed a persistent downward trend with minimal acid output of 9.5 at score 6. Statistical tests with ANOVA showed a significant difference between mean acid output among patients with different CISs (F = 6.9, p<0.5). Also, a significant inverse correlation of body combined

inflammation with acid output was apparent (CC = -0.50,  $p < 0.01$ ; fig 2).

Two other indices, body:antral chronic inflammation ratio and body:antral combined inflammation ratio were tested for their relationship with acid output. Both of them showed a significant inverse correlation with acid output, with CC = -0.49 ( $p < 0.01$ ). As shown in fig 3, the body:antrum ratio of active inflammation had a similar inverse correlation with acid output but with a relatively weak significance (CC = -0.17,  $p = 0.07$  and  $F = 3.0$ ,  $p = 0.05$ ).

The density of *H pylori* per each score of combined inflammation was also evaluated regarding relationship with acid output. Those indices at both antral and body sites were positively correlated with acid output with CC values of 0.29 ( $p < 0.01$ ) and 0.38 ( $p < 0.01$ ), respectively.

**Acid output and gastric atrophy**

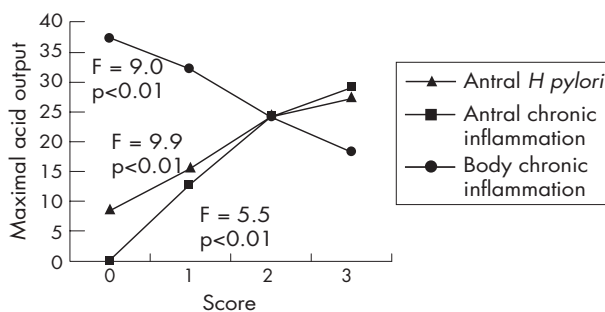
Antral-confined atrophy was detected in 19 (12.6%) patients and atrophy limited to the body in 27 (17.9%) patients. Only 11 (7.3%) patients had multifocal atrophy. Mean (SD) acid output in patients without atrophy was 29.1 (12.2) mmol/h. In patients with antral atrophy only, acid output was 19.5 (11.1), in patients with body atrophy only and multifocal atrophy, acid output was reduced at 11.5 (10.1) and 11.9 (7.2) mmol/h, respectively. Using one-way ANOVA, there were significant differences between groups regarding acid output ( $F = 22.0$ ,  $p < 0.01$ ). The Dunnett t test showed that acid output in each of the groups with atrophy was significantly different compared with the non-atrophic group (all  $p < 0.05$ ; fig 4).

As seen in fig 5, both antral and body atrophy scores had a significant inverse correlation with acid output. The CC for antral atrophy was -0.30 ( $p < 0.01$ ) and for body atrophy it was -0.59 ( $p < 0.01$ ). The ratio of body:antral atrophy also showed a prominent reverse relationship with acid output, with ratio  $< 1$  for an output of 27.4 mmol/h and ratio  $\geq 1$  for an output of 10.1 mmol/h (fig 6). Zero-order partial correlation showed that the relationship between body atrophy and acid output could be exaggerated with age and body-combined inflammation. After controlling for age, CC dropped from -0.54 to -0.48 (11% decrease). Controlling body-combined inflammation also decreased the CC of body atrophy score and acid output from -0.54 to -0.40 (26% decrease). By controlling both variables, CC dropped from -0.54 to -0.47 (31%).

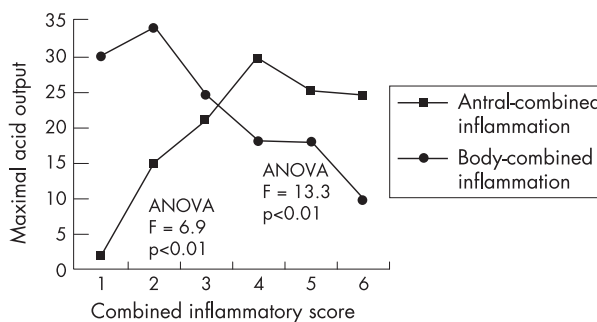
Intestinal metaplasia at both antral and body sites had a negative relationship with acid output with CC = 0.23 ( $p < 0.01$ ) and CC = 0.20 ( $p < 0.05$ ), respectively.

**Acid output and pepsinogen I, pepsinogen I:II ratio and gastrin-17**

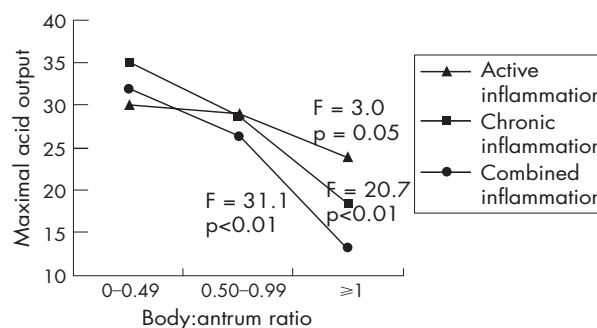
The median serum pepsinogen I and II concentrations of all participants were 73.5  $\mu\text{g/l}$  (IQR 48.5) and 9.6  $\mu\text{g/l}$  (IQR 8.0),



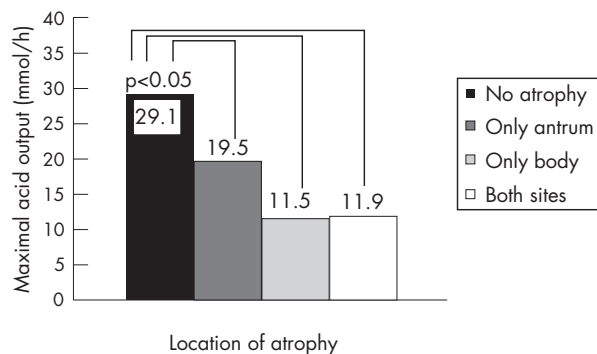
**Figure 1** Relationships of *Helicobacter pylori* (*H pylori*) infection, antral and body chronic inflammation with maximal acid output.



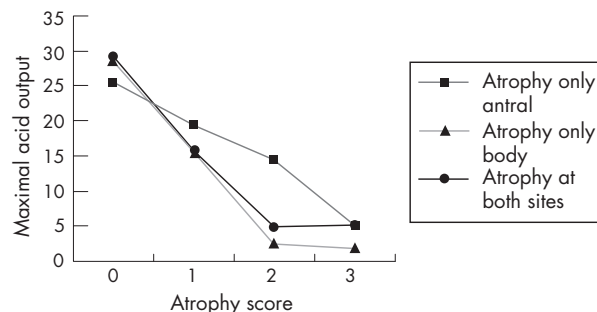
**Figure 2** Relationship of antral and body combined inflammation with maximal acid output.



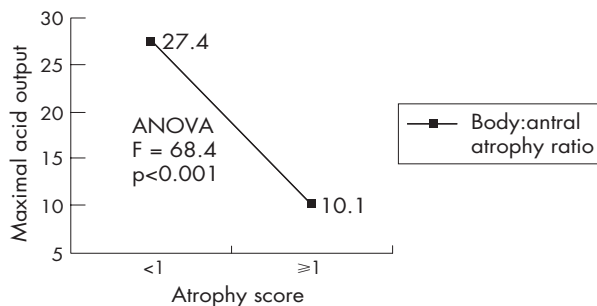
**Figure 3** Relationship of body:antrum ratios of active, chronic and combined inflammation with maximal acid output.



**Figure 4** Mean values of maximal acid output in patients with atrophy in different locations.



**Figure 5** Relationship of antral and body atrophy with maximal acid output.



**Figure 6** Relationship of body:antral atrophy ratio with maximal acid output. ANOVA, analysis of variance.

respectively. The calculated median pepsinogen I:II ratio was 7.6 (IQR 5.5). Serum pepsinogen I was positively correlated with acid output, with  $CC = 0.38$  ( $p < 0.01$ ). No relationship was found between acid output and serum pepsinogen II, but the ratio of pepsinogen I:II had a positive  $CC = 0.30$  ( $p < 0.01$ ) with acid output (figs 7, 8).

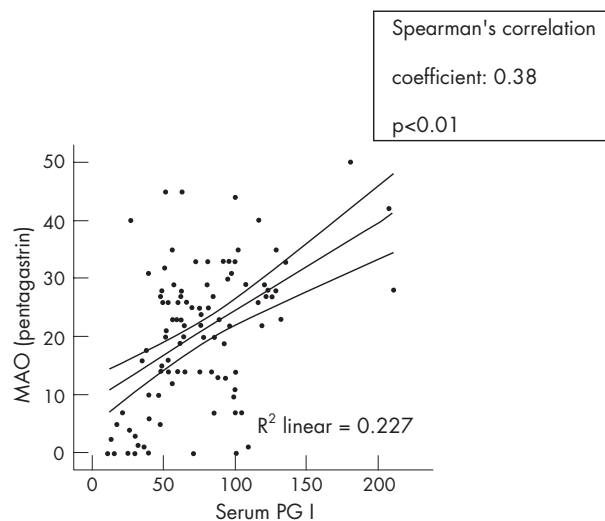
Median serum gastrin-17 of the enrolled patients was 2.2 pmol/l. There was no significant correlation between acid output and serum gastrin-17.

**CagA serology; relationship with acid output and gastric histology**

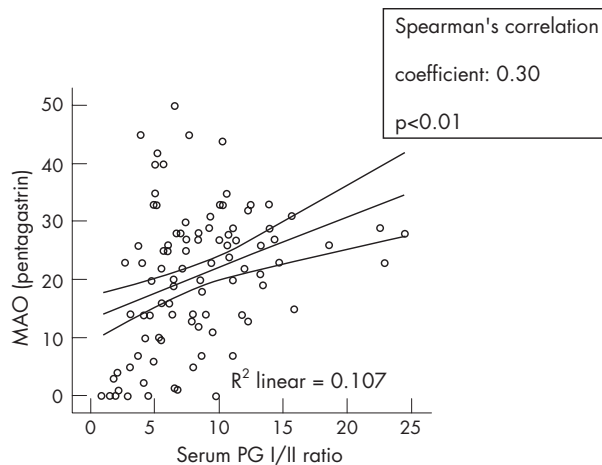
In 177 patients who had sufficient serum for anti-CagA serology, mean (SD) acid output was similar in patients with positive versus negative CagA serology with 28.3 (11.2) and 26.7 (12.3) mmol/h, respectively. However, there was a correlation between anti-CagA antibody titre and inflammatory histological parameters with respect to antral active inflammation ( $CC = 0.35$ ,  $p < 0.01$ ), body active inflammation ( $CC = 0.33$ ,  $p < 0.01$ ) and body chronic inflammation ( $CC = 0.24$ ,  $p < 0.05$ ). No significant relationship was found between anti-CagA antibody and atrophic or metaplastic changes in gastric mucosa.

**Other factors associated with acid output**

Age had an inverse relationship with acid output ( $CC = -0.44$ ,  $p < 0.01$ ; fig 9). Calculation of the relationship between acid output and age in men and women separately



**Figure 7** Relationship of serum pepsinogen I (PG I) with maximal acid output (MAO).



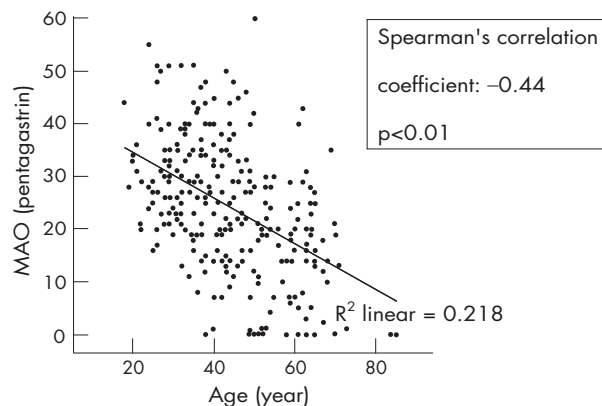
**Figure 8** Relationship of serum pepsinogen I:II ratio (PG I:II) with maximal acid output (MAO).

showed a slightly greater inverse relationship among men than among women ( $-0.41$  v  $-0.38$ ).

Regarding sex, men had mean (SD) acid output of 28.5 (13.2) mmol/h and women 21.4 (10.4) mmol/h. The difference with the independent t test was significant ( $p < 0.01$ ). Women were slightly older than men (median age 44 v 40 years, Mann-Whitney U test,  $p < 0.05$ ). Two other variables, body CIS and body atrophy were evaluated in both sexes, and we found no significant difference between men and women.

Smokers who smoked  $\geq 3$  cigarettes per day had mean (SD) acid output of 29.9 (9.1) mmol/h compared with non-smokers who had mean (SD) acid output of 26.5 (12.6) mmol/h. The difference between the two groups was at borderline significance ( $p = 0.05$ ). The major histological changes such as antral-combined inflammation, body-combined inflammation and body atrophy were not significantly different between smoker and non-smoker groups, but serum level of pepsinogen I was significantly higher in smokers than non-smokers (125.4 (IQR 58.5) v 95.3 (IQR 69)  $p < 0.05$ ).

The patient's height showed a positive significant correlation with acid output, with  $CC = 0.43$  and  $p < 0.01$ . Weight also had a positive but less potent relationship ( $CC = 0.26$ ,  $p < 0.01$ ) with acid output, but BMI did not show any significant relationship ( $CC = 0.02$ ,  $p = 0.84$ ). Sex subgroups were not different regarding the relationship of acid output and these variables.



**Figure 9** Relationship of age with maximal acid output (MAO).



**Best predictors of acid output**

To determine the best predictors of acid output, all variables, which had an obvious and marked linear relationship with acid, were selected. Body atrophy score, antral atrophy score, serum pepsinogen I, serum pepsinogen I:II ratio, serum gastrin, age, *H pylori* density of antrum and body, *H pylori* in one of the two sites and body CIS were entered as independent variables and acid output as dependent variable. The stepwise model produced four models. In the final model, according to standardised coefficients, body-combined inflammation ( $\beta = -0.34$ ), body atrophy ( $\beta = -0.30$ ), serum pepsinogen I ( $\beta = 0.26$ ) and age ( $\beta = -0.26$ ) were the most independent predictors of acid output. All other variables were excluded from the model according to enter and remove criteria. The R and R<sup>2</sup> in the final model were 0.79 and 0.62, respectively (table 1).

**DISCUSSION**

*H pylori* infection produces a wide variety of patterns of gastritis.<sup>33-42</sup> The pattern of gastritis varies in the extent to which it affects the antrum versus body region of the stomach and in the extent to which it produces acute inflammation, chronic inflammation, intestinal metaplasia and atrophy. Our study indicates that these different patterns of gastritis are associated with different levels of gastric acid secretion.

The antrum and body region of the stomach both have an important role in regulating gastric acid secretion. The antral mucosa contains the G cells, which release gastrin. This hormone is released in response to ingestion of protein-containing food and it stimulates the oxyntic mucosa to secrete acid.<sup>43</sup> The hormone acts on the gastrin receptors on the enterochromaffin-like (ECL) cells of the oxyntic mucosa causing them to release histamine, which acts in a paracrine fashion, binding to the H<sub>2</sub> receptors on the parietal cells and thereby stimulating them to secrete acid.<sup>44-46</sup> Gastrin also exerts a trophic influence on the ECL cells and parietal cells of the oxyntic mucosa.<sup>47 48</sup>

*H pylori* gastritis influences the function of the antral mucosa, stimulating an increased release of gastrin by the G cells.<sup>27 49-52</sup> It is unclear whether this is due to the influence of inflammatory cytokines<sup>53-55</sup> or the ammonia produced by the urease activity of the bacterium, raising antral surface pH and thus blocking the physiological inhibition of gastrin release by luminal acid.<sup>56</sup> *H pylori* antral gastritis will thus tend to increase gastric acid secretion by increasing gastrin release. If the infection produces atrophy of the antral mucosa, the rise in gastrin will be moderated due to loss of G cells.<sup>57 58 28</sup> As gastrin is released by ingestion of food, the main influence of the antrum is in meal-stimulating acid secretion, which is technically difficult to measure. We assessed acid secretion in response to stimulation by exogenous gastrin, which acts

directly on the oxyntic mucosa. Our study will therefore not have detected changes in meal-stimulated acid secretion due to disturbances in antral function.

Our study shows the strong correlation between *H pylori* body gastritis and reduced gastric acid secretion. Both inflammation and atrophy of the body mucosa were strongly associated with reduced gastric acid secretion. The effect of the atrophy is clearly explained by loss of acid-secreting parietal cells. The inflammation of the body mucosa is thought to produce functional inhibition of acid secretion. We, and others, have shown that eradicating *H pylori* in patients with low acid secretion produces recovery of secretion, which is associated with resolution of the body gastritis without any change in atrophy.<sup>28 59</sup> The mechanism by which *H pylori*-induced inflammation impairs the function of the oxyntic mucosa is not clear. However, the infection stimulates production of interleukin 1 $\beta$ , which is a powerful inhibitor of acid secretion, blocking the release of histamine from the ECL cells and also inhibiting the function of the parietal cells.<sup>60 61</sup> Our study clearly shows that atrophy and inflammation are both independently associated with low acid secretion.

The serum concentrations of pepsinogens are indicators of gastric atrophy and consequently of gastric secretory function. Pepsinogen I originates from gastric fundic glands,<sup>62</sup> whereas pepsinogen II is secreted by glands of the body and antral region of the stomach as well as the proximal duodenum.<sup>63</sup> We found pepsinogen I to be the most useful predictor of the disturbance of acid secretion in our patients infected with *H pylori*. This is consistent with our histological studies confirming that atrophy of the body mucosa was the most powerful predictor of low acid secretion, as pepsinogen I is a strong predictor of body atrophy.

We also examined the influence of a variety of demographic characteristics of the patients on acid secretion. Our data showed that smokers who smoked  $\geq 3$  cigarettes per day had greater acid secretion than non-smokers. We found no significant relationship between cigarette smoking and major histological factors, but our data showed a higher level of pepsinogen I among smokers. Chronic smoking is associated with higher gastric acid secretion in subjects with and without ulcer.<sup>64-67</sup> In addition, there is a significant positive association between the number of cigarettes smoked and the magnitude of acid secretion.<sup>68</sup> Nicotine administered intravenously stimulates acid secretion in humans.<sup>69</sup> Chronic cigarette smoking stimulates the vagus and activates the parietal cells to enhance acid output.<sup>68</sup> Increased serum pepsinogen I in smokers was another finding of our study, which could be related to their higher acid secretion with a parallel increase in chief cell secretory capacity.<sup>65</sup>

Our data indicate a marked decline in acid secretion with increasing age in male and female patients infected with *H*

**Table 1** Summary of stepwise linear regression analysis for predictors of maximal acid output

Predictors	Unstandardised coefficients		Standardised coefficients	p Value	Collinearity statistics	
	B	SE	$\beta$		Tolerance*	VIF†
Intercept (constant)	42.38	7.00		0.00		
Body combined Inflammation	-2.56	0.79	-0.34	0.00	67	1.50
Body atrophy	-5.44	1.94	-0.30	0.01	63	1.60
Age	-0.33	0.11	-0.26	0.00	97	1.04
Serum pepsinogen I	0.04	0.01	0.26	0.01	86	1.16

Dependent variable: maximal acid output.  
R = 0.79, R<sup>2</sup> = 0.62, SE of the estimate = 8.43

\*Tolerance is the percentage of the variance in a given predictor that cannot be explained by other predictors.

†A variance inflation factor (VIF) >2 is usually considered problematic regarding collinearity with other predictors.

*pylori*. The median acid output in 20-year-olds was 35 mmol/h, which fell to 15 mmol/h in 70-year-olds. This negative association between acid secretion and age in patients infected with *H pylori* has been previously observed.<sup>70</sup> By contrast, acid output has been reported to remain steady or increase with age in patients infected with *H pylori*.<sup>71</sup> The lower acid secretion in the older patients infected with *H pylori* can be explained partly (but not completely) by more severe body gastritis and higher prevalence of atrophy.<sup>70 72 73</sup> It is unclear to what extent the higher prevalence of low acid secretion and that of body gastritis and atrophy in older patients is due to increasing age or a cohort effect, where those born at an earlier time have increased predisposition to develop these abnormalities. In some patients with severe body atrophy, autoimmune gastritis may be an aetiological factor for hypochlorhydria in advanced age. This may result as a consequence of the interaction between *H pylori* infection and host response to the organism's antigens, and to gastric autoantigens including gastric H+K+ATPase.<sup>74</sup>

Our study showed that male patients have greater acid output than females. This finding is consistent with previous work,<sup>75 76</sup> but its biological explanation has not been clearly defined. In women, smaller gastric surface area and corresponding smaller parietal cell mass or lower parietal cell reactivity or both may be responsible.<sup>76-78</sup> The patient's height positively correlated with acid output, and this effect was similar in both sexes, suggesting that body surface may explain the greater acid secretion in men. Iijima *et al*<sup>70</sup> reported that in subjects infected with *H pylori*, there was a more marked fall in acid output with increasing age in men versus women. This is consistent with our finding.

Owing to the number and variety of factors affecting acid secretion and the potential for interaction between them, we carried out stepwise linear regression analysis. This indicated four independent factors, (1) body inflammation, (2) body atrophy, (3) serum pepsinogen I and (4) age, as powerful predictors of acid secretion. A combination of these factors had a strong relationship with acid output and could be used for prediction of acid output in individual patients.

It should be emphasised that this study shows the association between the patterns of gastritis and gastric acid secretion but does not in itself indicate the nature of the association. Previous studies<sup>28 79 80</sup> have shown that eradication of *H pylori* infection causes recovery of gastric acid secretion in patients with body-predominant atrophic gastritis, thereby providing evidence that this histological pattern of gastritis can inhibit acid secretion. However, it is important to recognise also that acid secretion may affect the pattern of gastritis. This is shown by the fact that inhibition of acid secretion by proton pump inhibitors causes the pattern of gastritis to change from an antral-predominant gastritis to a body-predominant gastritis and may also cause acceleration of the atrophic process.<sup>81</sup>

Irrespective of the complex nature of the association between the pattern of gastritis and acid secretion, our study provides data allowing the prediction of acid secretion based on gastric histology, serological markers and patient characteristics. This may be useful in estimating levels of acid secretion in different populations as well as in individual patients.

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Competing interests: None declared.

This study was approved by the Ethics Committee of the Western Infirmary, Glasgow, UK.

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