Non-endoscopic diagnosis of atrophic gastritis with a blood test. Correlation between gastric histology and serum levels of gastrin-17 and pepsinogen I: a multicentre study

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Background and aims **Serum levels of gastrin-17 (S-G-17) and pepsinogen I (S-PGI) are biomarkers of gastric antral and corpus mucosa, respectively. In a prospective multicentre investigation, we determined whether these tests, together with the assay of *Helicobacter pylori* antibodies, are a non-endoscopic tool for the diagnosis of atrophic gastritis.**

Materials and methods **The series comprised 404 consecutive adult outpatients undergoing diagnostic upper-gastrointestinal endoscopy for various dyspeptic symptoms in five outpatient clinics. Gastric biopsies from the antrum and corpus (at least two biopsies from both sites) were available from all patients, and they were evaluated according to the guidelines of the updated Sydney system. S-PGI and S-G-17 were assayed with ELISA methods using monoclonal antibodies to pepsinogen I and amidated gastrin-17. In addition to the fasting level (S-G-17_{fast}), a postprandial S-G-17 (S-G-17_{prand}) level was measured 20 min after ingestion of a protein-rich drink. *H. pylori* antibodies were determined using a polyclonal EIA method.**

Results **S-G-17_{prand} (and S-G-17_{fast}) and S-PGI levels decreased with increasing grade of atrophy of the antrum or corpus, respectively. S-G-17_{prand} levels were significantly lower in patients with advanced (moderate or severe) atrophic antral *H. pylori* gastritis than in those with non-atrophic *H. pylori* gastritis. All patients with a resected antrum demonstrated S-G-17_{prand} levels that were almost undetectable. Of the nine patients with an *H. pylori*-positive moderate or severe atrophic antral gastritis, six had S-G-17_{prand} levels below 5 pmol/l. Similarly, S-PGI levels were significantly lower in patients with advanced corpus atrophy than in those without. Of the 45 patients with moderate or severe corpus atrophy in endoscopic biopsies, 35 patients had S-PGI levels < 25 μg/l. By using the cut-off levels for S-G-17_{prand} and S-PGI with the best discrimination, the sensitivity and specificity of the blood test panel in delineation of patients with advanced atrophic gastritis (either in the antrum or the corpus, or both) were 83% and 95%, respectively. The predictive values of the positive and negative test results were 75% and 97%, respectively. In the diagnosis of atrophic gastritis, the application of S-G-17_{fast} showed a slightly lower sensitivity and specificity than the application of S-G-17_{prand} as a biomarker for antral atrophy.**

Conclusions **The diagnosis of atrophic gastritis obtained with the blood test panel of S-G-17, S-PGI and *H. pylori* antibodies is in good agreement with the endoscopic and biopsy findings. The panel is a tool for non-endoscopic diagnosis and screening of atrophic gastritis. *Eur J Gastroenterol Hepatol* 15:885–891 © 2003 Lippincott Williams & Wilkins**

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Introduction

According to the statements of the Maastricht 2000 Consensus, atrophic gastritis is an indication for the eradication of *Helicobacter pylori* if these two conditions coincide [1]. Measurements of the serum levels of pepsinogen I (S-PGI) or the ratio of pepsinogen I to pepsinogen II (PGI/PGII) are well-known non-endoscopic tools for diagnosing atrophic gastritis of the gastric corpus [1–8]. With worsening of corpus atrophy (loss of normal oxyntic glands), S-PGI and PGI/PGII tend to decrease. Recent studies [9,10] indicate that assays of serum levels of gastrin, particularly gastrin-17 (G-17), could be used as an indicator of the morphological status of the antral mucosa, i.e. a low serum G-17

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(S-G-17) is a biomarker of atrophic antral gastritis (loss of antral G-cells).

The aim of the present investigation was to study in a prospective multicentre approach whether patients with atrophic gastritis can be found non-endoscopically using a test panel (GastroPanel, Biohit Plc, Helsinki, Finland) employing the concomitant assays of S-PGI and S-G-17 as well as *H. pylori* antibodies.

Materials and methods

Study population

The study was a multicentre approach and consisted of 404 consecutive outpatients who were endoscoped for various dyspeptic symptoms in five outpatient centres in southern Finland in 2001. The mean age was 58 ± 15 years, and the male/female ratio was 164/240. The blood tests were assayed in most patients within two weeks after endoscopy. The patients were asked to not use treatments affecting the acid output (H_2 blockers, proton pump inhibitors, antacids, etc.) one week before the blood test if possible.

Endoscopy and biopsy sampling

Diagnostic upper-gastrointestinal endoscopy (gastroscopy) was performed in all patients at least one day before the laboratory tests. Random biopsies were obtained from the antrum and corpus, with at least two biopsies from each site in addition to biopsies from endoscopically visible mucosal lesions. The random biopsies were taken from the lesser and greater curvatures of the middle antrum. The corpus biopsies were from the anterior and posterior walls of the middle corpus.

The biopsy specimens were processed into paraffin blocks, and histological sections were obtained using ordinary methods and stains [haematoxylin–eosin, modified Giemsa and Alcian blue (pH 2.5), periodic acid Schiff reagent (PAS)]. *H. pylori*, chronic inflammation, activity, atrophy, and intestinal metaplasia were noted and graded by the principles of the updated Sydney system and analogue visual scale.

Based on the histological appearances, the patients were classified into the following groups:

- *Normal and healthy gastric mucosa (N):* no gastritis, no atrophy.
- *Non-atrophic gastritis (non-AG):* presence of *H. pylori* gastritis without biopsy evidence of advanced atrophy or intestinal metaplasia. This category was not subdivided into antral- or corpus-predominant gastritis. It also includes cases in which the degree of atrophy and intestinal metaplasia was obscure or mild at most.
- *Advanced atrophic gastritis in antrum (A), corpus (C) or both (AC; multifocal atrophic gastritis):* presence of moderate or severe atrophy (loss of normal glands) in the antrum or the corpus, or both, respectively. Moderate and severe atrophy were considered to be clinically significant, and relevant stages can be quite reliably diagnosed and categorized by a limited number of endoscopic biopsies. These stages of atrophy represent conditions in which the number of normal antral or corpus (oxyntic) glands is diminished by at least half. Intestinal metaplasia was used as an additional indicator for atrophy, in particular in the antrum, i.e. the presence of intestinal metaplasia suggests the loss of glands and atrophy. Atrophy was considered to be advanced (moderate or severe) in antral biopsies if at least half of the normal glands and epithelium were replaced by intestinal metaplasia in the available biopsy specimens.

Blood samples

The basal blood samples for measurements of PGI, fasting (basal) gastrin-17 ($G\text{-}17_{fast}$) and immunoglobulin G (IgG) antibodies to *H. pylori* were drawn after an overnight fast. The sample for postprandial gastrin-17 ($G\text{-}17_{prand}$) was taken 20 min after a protein drink (10 g protein, Biohit Plc). The samples were collected into serum tubes. These blood tubes were centrifuged at 1500 ***g*** for 10 min, and the serum samples were stored at −70°C until they were analysed.

Diagnosis of atrophic gastritis by the blood test panel

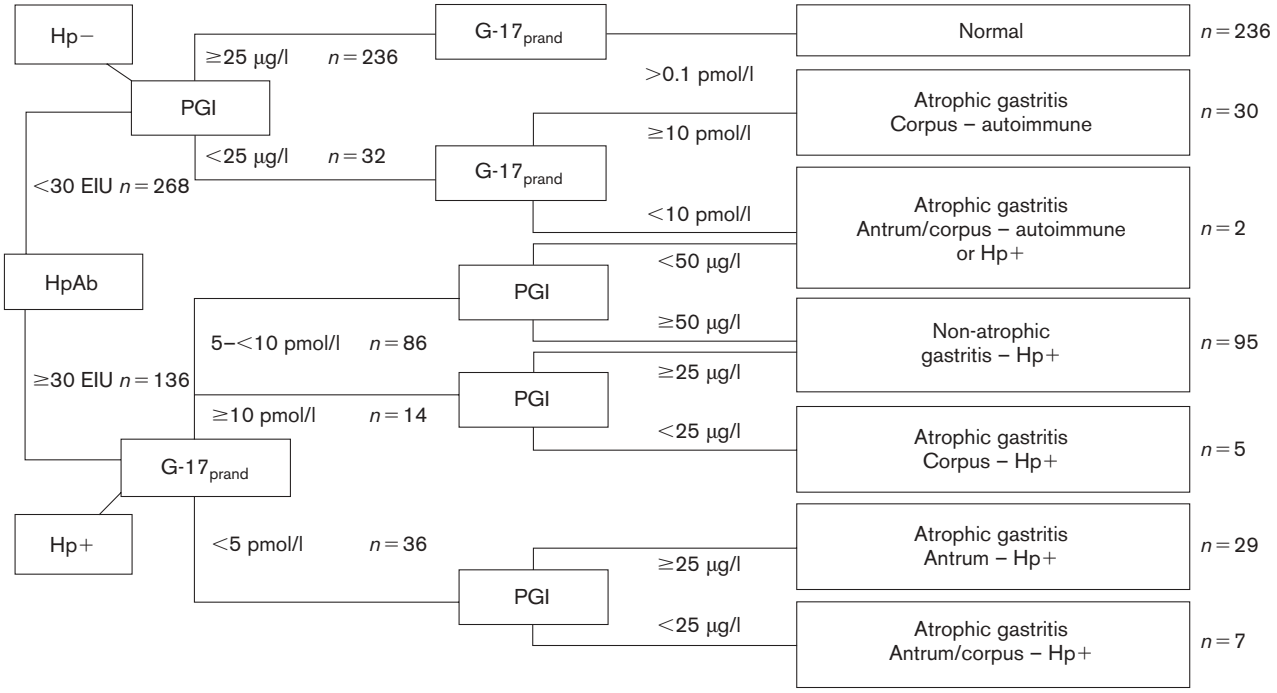
In delineation of patients with different topographic types of atrophic gastritis with the blood test panel, an algorithm and a computer program (GastroSoft, Biohit Plc) were used. These criteria for the best discrimination of gastritis of different types were obtained from previous studies [9] (see also www.biohit.com/gastrosoft). This algorithm and the different topographic types of atrophic gastritis are presented in Figure 1. This shows the cut-off values for the panel that uses $S\text{-}G\text{-}17_{prand}$ as a biomarker for antral atrophy. When $S\text{-}G\text{-}17_{fast}$ is applied as a marker for antral atrophy, the cut-off values of S-G-17 are half of those shown in the algorithm for $S\text{-}G\text{-}17_{prand}$. The cut-off values of S-PGI and *H. pylori* antibodies are the same, irrespective of whether $S\text{-}G\text{-}17_{prand}$ or $S\text{-}G\text{-}17_{fast}$ is applied.

Laboratory tests

G-17, PGI and IgG class antibodies to *H. pylori* were determined using specific EIA tests (Gastrin-17 EIA Test Kit, Pepsinogen-I EIA Test Kit and *Helicobacter pylori* IgG EIA Test Kit, Biohit Plc) and were performed in batches of 40 samples on a microwell plate according to the instructions of the manufacturer.

All EIA techniques were based on measuring the absorbance after a peroxidation reaction at 450 nm.

Fig. 1



Algorithm (decision tree) for classification of patients into different categories of atrophic gastritis by the *Helicobacter pylori* antibody titre (HpAb) and serum levels of pepsinogen I (PGI) and postprandial gastrin-17 ($G\text{-}17_{prand}$). When $S\text{-}G\text{-}17_{fast}$ is applied as a biomarker for antral atrophy, the cut-off values of S-G-17 are half of those shown in the algorithm for $S\text{-}G\text{-}17_{prand}$. The cut-off values of S-PGI and HpAb are the same, irrespective of whether $S\text{-}G\text{-}17_{prand}$ or $S\text{-}G\text{-}17_{fast}$ is applied. The absence of evidence of *H. pylori* infection is considered to indicate an autoimmune origin of gastritis. The number of cases in each arm of the algorithm is indicated.

Between the reaction steps, the plates were washed using a BW50 Microplate Strip Washer (Biohit Plc). The absorbances were measured using a microwell plate reader (BP800 Microplate Reader, Biohit Plc). For determination of PGI and G-17 values, second-order fits on standard concentrations were used to interpolate/extrapolate unknown sample concentrations automatically with the help of the BP800 built-in software. The *H. pylori* antibodies were expressed as enzyme immuno-units (EIU) according to the formula included in the test kit (sample $EIU = [X(A_{Sample}) - X(A_{Blank})]/[X(A_{Calibrator}) - X(A_{Blank})]$). EIU levels of 30 and above were considered to be *H. pylori*-positive.

Specificity of laboratory tests

The monoclonal antibodies of G-17 and PGI used in the EIA tests were highly specific. The G-17 antibody detected only amidated gastrin-17 and no other gastrin molecules or fragments (e.g. glycine-extended gastrin-17, a kind gift from Prof. Jens F. Rehfeld, Copenhagen, Denmark; human synthetic gastrin-34, G-5024, Sigma, USA; human synthetic gastrin-13, G-0267, Sigma; or cholecystokinin (CCK) fragment 26-33 amide, C-2901, Sigma). The antibodies were also applicable in immunohistochemistry (formalin-fixed, paraffin-embedded specimens) in dilutions up to 10 000. In immunohistochemistry, the G-17 antibodies stained only antral G-cells and glands, but no other cells or tissues in the stomach, duodenum, small or large bowel, or pancreas. This specificity was also the case with the PGI antibody, which stained only chief and neck cells of the gastric corpus (oxyntic gland mucosa).

The PGI and *H. pylori* antibody EIA tests had a high correlation with the results of other commercial tests (PEPSI-I K RIA, DiaSorin, Rome, Italy; Gastroset PG I EIA, Orion Diagnostica, Helsinki, Finland; Pyloriset EIA-G III, Orion Diagnostica). The G-17 EIA results correlated well with those of the G-17 RIA (courtesy of Prof. Jens F. Rehfeld and Dr Jens-Peter Gotze, Copenhagen, Denmark).

Statistics

Non-parametric tests (Wilcoxon–Mann–Whitney test, SPSS 10.1 software) were used in the calculations of the significance between the groups. For prevalence and mean values, 95% confidence intervals (CI) and standard deviations (SD) were estimated on the basis of binomial and normal distribution. In using the *t*-test, G-17 and PGI values were transformed logarithmically (ln).

Ethics

The study was accepted by the Ethical Committee of the Helsinki District University Hospital, Helsinki, Finland. The purpose of the study was explained to all patients before taking the blood samples, and all patients signed a written consent form before enrolment into the study.

Results

H. pylori positivity and endoscopy findings in the study population

The study population consisted of 404 patients collected prospectively from those endoscopied for dyspeptic symptoms in five centres in southern Finland in 2001. Of these patients, 136 (34%) were *H. pylori*-positive in serology (*H. pylori* antibodies EIU ≥ 30), including eight patients in whom the EIU of *H. pylori* antibodies was below the cut-off value but in whom an eradication of *H. pylori* was done within two years previously. In patient groups with N, non-AG, C, AC or A (including R) by endoscopy/histology, the *H. pylori* seropositivity occurred in 16/223 (7%), 94/115 (82%), 8/40 (20%), 3/4 (75%) and 15/22 (68%) patients, respectively.

In patients with non-atrophic gastritis (non-AG) compared with those with normal gastric mucosa (N), the fasting G-17 and PGI levels in serum were 8.4 pmol/l (SD 15.6) versus 3.9 pmol/l (SD 5.3), and 209 μg/l (SD 163) versus 145 μg/l (SD 113), respectively. Serum levels of postprandial G-17 in the corresponding two groups were 25.2 pmol/l (SD 28.9) and 14.8 pmol/l (SD 17.3), respectively.

At endoscopy, 13 patients showed an active duodenal ulcer and ten an active gastric ulcer. Four of these duodenal ulcers and three of the gastric ulcers were associated with a normal, healthy stomach (N) and one with an antrum-limited atrophic gastritis (A), according to the gastric biopsy specimens. The rest were in patients with non-atrophic gastritis (non-AG). A definite dysplastic lesion of low grade was diagnosed in the stomach of one patient and in the duodenum of another, the first one showing non-AG gastric histology. The patient with duodenal adenoma and low-grade dysplasia exhibited normal endoscopy and histology but was categorized into group A by the GastroPanel. There were no carcinomas in the oesophagus or the stomach (all patients with suspected malignancy or diseases that need immediate treatments other than with medications were excluded from the present series). Eighteen patients showed a long or short segment of Barrett's oesophagus or ulcerative oesophagitis based on endoscopy and biopsy findings. Of these, 12 were categorized into the endoscopy/histology group N, five into the group non-AG, and one into the group A. One patient had suspected Crohn's disease of the stomach.

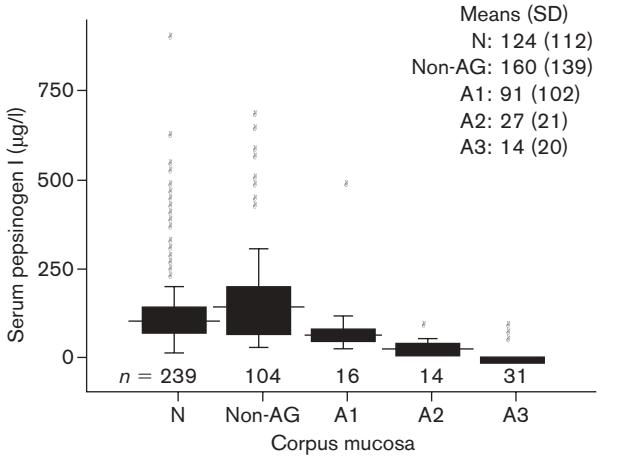
Serum pepsinogen I and gastrin-17

S-PGI levels decreased with increasing grade of atrophy (atrophic gastritis) in the corpus mucosa (Fig. 2). Of the 45 patients with moderate or severe corpus atrophy, 35 had S-PGI levels below 25 μg/l. Correspondingly, S-G-17_{prand} and S-G-17_{fast} decreased with increasing grade of antral atrophy (Figs 3 and 4). The mean and median values of S-PGI and S-G-17_{prand} were significantly lower in patients with moderate or severe corpus or antral atrophy than in those without atrophic gastritis or with non-atrophic *H. pylori* gastritis ($P < 0.01$; Wilcoxon–Mann–Whitney test and *t*-test after ln transformation) (Figs 2 and 3). In all five patients with previous antrectomy S-G-17_{prand} was almost zero (mean 0.12 pmol/l (SD 0.27)).

Blood test panel

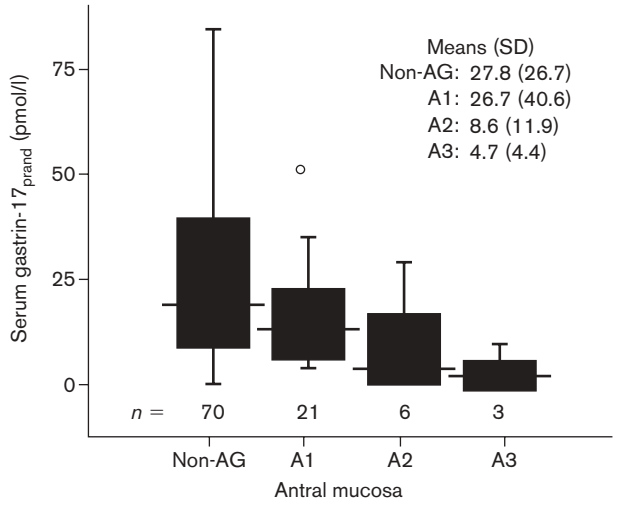
The results of the comparison of the endoscopy and biopsy diagnosis with the diagnosis of different topographic phenotypes of gastritis or atrophic gastritis obtained by the test panel and the algorithm are presented in Figure 1 and Tables 1 and 2. Table 1 and Figure 1 show the results in which S-G-17_{prand} was used as a marker of antral mucosa. Table 2 presents the corresponding results when S-G-17_{fast} was used instead of S-G-17_{prand}.

Fig. 2



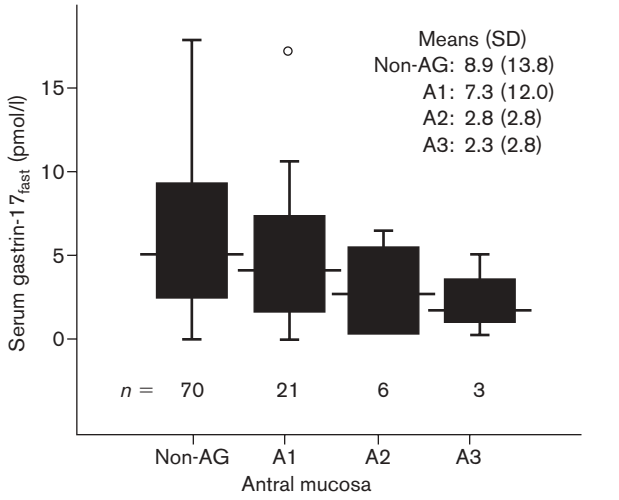
Box-plot presentation of pepsinogen I and atrophy in the corpus mucosa. The black horizontal line inside the box marks the median value. The length of the box shows the range within which the middle 50% of the values fall. The whiskers show the range of values that fall within 1.5× difference of the values of the two hinges of the box. Outlying values are also indicated. Means (SD) are shown separately. A1, mild atrophic gastritis; A2, moderate atrophic gastritis; A3, severe atrophic gastritis; N, normal and healthy gastric mucosa; Non-AG, non-atrophic ('superficial') gastritis.

Fig. 3



Box-plot presentation (see Fig. 2 for details) of postprandial levels of serum gastrin-17 (S-G-17_{prand}) and atrophy in the antral mucosa. Patients with *Helicobacter pylori* infection (HpAb ⩾ 30 enzyme immuno-units) and normal serum level of pepsinogen I (S-PGI ⩾ 25 μg/l). Means (SD) are shown separately.
A1, mild atrophic gastritis; A2, moderate atrophic gastritis; A3, severe atrophic gastritis; N, normal and healthy gastric mucosa; Non-AG, non-atrophic ('superficial') gastritis.

Fig. 4



Box-plot presentation (see Fig. 2 for details) of basal, fasting levels of serum gastrin-17 (S-G-17_{fast}) and atrophy in the antral mucosa. Patients with *H. pylori* infection (HpAb ⩾ 30 enzyme immuno-units) and normal serum level of pepsinogen I (S-PGI ⩾ 25 μg/l). Means (SD) are shown separately.
A1, mild atrophic gastritis; A2, moderate atrophic gastritis; A3, severe atrophic gastritis; N, normal and healthy gastric mucosa; Non-AG, non-atrophic ('superficial') gastritis.

The overall accuracy of the test panels using S-G-17_{prand} or S-G-17_{fast} as a biomarker of gastric antrum was 83% (74–92%) and 81% (77–85%), respectively. In delineation of patients with advanced (moderate or severe) atrophic gastritis in the antrum or the corpus, or both, the sensitivity and specificity of the test panel were high. These figures, including the values of positive and negative test results to predict correct diagnosis, are presented in Table 3. The test panel including S-G-17_{prand} showed slightly better results than the panel including S-G-17_{fast}. S-G-17_{prand} and S-G-17_{fast} had a significant correlation. After ingestion of the protein-rich drink, S-G-17_{prand} levels were approximately twice as high as S-G-17_{fast} levels.

Discussion

The present study indicates that, in association with *H. pylori* testing, the serum levels of G-17 and PGI can be used as biomarkers of gastritis and atrophic gastritis in the antrum or corpus, respectively. In the present study, S-G-17 decreased with increasing grade of antral atrophy among *H. pylori*-infected patients, and all patients with resected antrum (previous antrectomy for peptic ulcer disease) had almost unmeasurable levels of S-G-17. Correspondingly, S-PGI decreased with increasing grade of corpus atrophy in a way that has been demonstrated in many previous studies [2–8]. By using all three blood tests (*H. pylori* antibody assay, S-G-17, S-PGI) as a panel and by using the GastroSoft compu-

Table 1 Correlation between diagnoses obtained with endoscopy (and histology) and those obtained with the blood test panel (GastroPanel). The panel includes assay of postprandial serum levels of gastrin-17 (protein-rich drink; S-G-17_{prand})

	Endoscopy and histology						
GastroPanel	R	A	AC	C	Non-AG	N	Total
A	4	10	0	0	11	4	29
AC	2	0	3	2	1	1	9
C	0	1	1	32	0	1	35
Non-AG	0	2	0	2	81	10	95
N	0	3	0	4	22	207	236
Total	6	16	4	40	115	223	404

A, advanced (moderate or severe) atrophy in antrum alone; AC, advanced (moderate or severe) atrophy in both antrum and corpus; C, advanced (moderate or severe) atrophy in corpus alone; N, normal and healthy antrum and corpus mucosa; Non-AG, non-atrophic ('superficial') gastritis; R, resected antrum.

Table 2 Correlation between diagnoses obtained with endoscopy (and histology) and those obtained with the blood test panel. The panel includes assay of basal fasting serum levels of gastrin-17 (S-G-17_{fast})

	Endoscopy and histology						
GastroPanel	R	A	AC	C	Non-AG	N	Total
A	4	9	0	0	20	5	38
AC	2	0	1	2	2	1	8
C	0	1	1	32	0	1	35
Non-AG	0	2	1	2	71	9	85
N	0	4	1	4	22	207	238
Total	6	16	4	40	115	223	404

A, advanced (moderate or severe) atrophy in antrum alone; AC, advanced (moderate or severe) atrophy in both antrum and corpus; C, advanced (moderate or severe) atrophy in corpus alone; N, normal and healthy antrum and corpus mucosa; Non-AG, non-atrophic ('superficial') gastritis; R, resected antrum.

Table 3 Accuracy of the test panel in the diagnosis of advanced atrophic gastritis. Panels include assays of postprandial (after stimulation with protein-rich drink) serum gastrin-17 (S-G-17$_{prand}$) or basal fasting serum gastrin-17 (S-G-17$_{fast}$)

	Panel (S-G-17$_{prand}$)	Panel (S-G-17$_{fast}$)
Overall accuracy	83% (74–92%)	81% (77–85%)
Diagnosis of atrophic gastritis		
Sensitivity	83% (74–92%)	79% (69–89%)
Specificity	95% (92–97%)	91% (88–94%)
PPV	75% (65–85%)	64% (54–75%)
NPV	97% (95–99%)	93% (90–96%)

NPV, predictive value of the negative test result; PPV, predictive value of the positive test result.
95% confidence intervals are indicated in parentheses. The overall accuracy was calculated from Tables 1 and 2 as a proportion of the cases that totally fitted between the GastroPanel and the endoscopy/histology. In calculations of the sensitivity of the GastroPanel to diagnose atrophic gastritis (categories R, A, AC and C combined), the sensitivity indicates the proportion of cases that the GastroPanel could find among those with atrophic gastritis in endoscopy/histology. Correspondingly, the specificity indicates the proportion of those patients in whom the GastroPanel indicated non-atrophic gastritis (N or non-AG) among those who had normal (N) or non-atrophic gastritis (non-AG) in endoscopy/histology.

ter program to generate the diagnosis, it was possible to delineate the patients with advanced atrophic gastritis (either in the antrum or the corpus, or both) with a reasonably high accuracy. The data from the present prospective study among dyspeptic outpatients are comparable with those from our earlier observational case–control-type study [9] and with those of an earlier prospective Italian study [10]. These three studies suggest that the overall accuracy of the panel in the diagnosis of atrophic gastritis is approximately 80% when compared with the diagnosis from endoscopy and biopsies. It seems that, in addition to disclosing patients with severe atrophic corpus gastritis, the panel enables the delineation and diagnosis of patients who have advanced atrophic gastritis only in the antrum or in both the antrum and the corpus (multifocal atrophic gastritis).

The decrease in S-G-17 and S-PGI as atrophic gastritis worsens is certainly based on a loss of normal mucosal glands and cells in the antrum and corpus mucosa. G-17 is synthesized and secreted almost solely from antral G-cells [11]. These cells are constituents of normal antral (pyloric) glands, and during the progression and worsening of the atrophic gastritis they disappear with the disappearance of the antral glands and with the extension of intestinal metaplasia and pseudopyloric metaplasia in the antrum. In spite of this simple background, the serum levels of G-17 are also influenced by the presence or absence of inflammation (*H. pylori* gastritis) in the stomach, by intragastric acidity, and by various physiological stimuli. Therefore, in the consideration of S-G-17 as a biomarker of antral mucosa, the presence or absence of *H. pylori* gastritis and the grade of atrophy in the corpus mucosa (S-PGI) have to be taken into consideration simultaneously. This means that *H. pylori*, S-G-17 and S-PGI, when assayed concomitantly, form a test panel, and the final diagnosis has to be based on a decision-tree-like algorithm and on empirical cut-off levels with best discrimination for the three test parameters.

H. pylori gastritis tends to raise the serum levels of G-17 and PGI, and a low intragastric acidity increases the serum levels of G-17, and vice versa. Permanent, long-lasting hypo- or achlorhydria results in extremely high levels of G-17 in the circulation, possibly due to hyperplasia of the antral G-cells [12]. This occurs particularly in patients in whom the hypoacidity (atrophic gastritis in the corpus) occurs in connection with non-atrophic antrum, which is often the case in patients with autoimmune atrophic corpus gastritis [12]. If the antral mucosa is concomitantly atrophic (multifocal atrophic gastritis), the S-G-17 level does not rise and the blood test panel shows both low S-PGI and low S-G-17 values [13].

Due to the known physiological background and feedback mechanisms in the control of acid and gastrin secretion, a logical decision tree (algorithm) can be constructed for the test panel to depict patients with different phenotypes of gastritis and atrophic gastritis [9]. This decision tree begins with the consideration whether the patient has *H. pylori* infection with consequent gastritis. If there is neither infection nor gastritis, then a low S-PGI (empirical cut-off with best discrimination < 25 μg/l) indicates advanced atrophic corpus gastritis that may be autoimmune in origin (or a previous *H. pylori* infection has healed spontaneously). Correspondingly, normal S-PGI levels in these patients suggest that the stomach is normal and healthy. In association with *H. pylori* infection and gastritis, a low S-PGI level suggests that the atrophic corpus gastritis is bacterial in origin, and that this infection should be treated as recommended recently by the Maastricht 2000 Consensus Statement [1]. Correspondingly, a low S-G-17 level (S-G-17$_{prand} < 5$ pmol/l) in connection with *H. pylori* infection indicates advanced atrophic gastritis in the antrum. If the antrum and corpus are concomitantly atrophic, even somewhat higher S-G-17 levels (S-G-17$_{prand} < 10$ pmol/l) also suggest antral atrophy. In *H. pylori*-positive patients, 'normal' S-PGI (> 50 μg/l) and S-G-17 (S-G-17$_{prand} < 5$ pmol/l) levels indicate strongly and reliably that the gastritis is non-atrophic and that the acid output is obviously normal or high. These are the patients in whom the risk of peptic ulcer disease is increased but the risk of gastric cancer is lower than expected (i.e. lower than the average cancer risk in the general population) [14].

In the present series, 15/29 patients with non-atrophic antral gastritis or normal stomach were misclassified as patients with atrophic antral gastritis by the GastroPanel. It is possible that acid secretion was high in these

patients. The high intragastric acidity may inhibit the release of G-17 from antral G-cells, resulting in low serum levels of G-17 even postprandially and in false interpretation of the presence of antral atrophy. However, these may be the patients in whom the risk of acid-related duodenogastric or gastro-oesophageal diseases is highest.

The overall G-17 levels in the serum are low in normal circumstances, and gastrins are easily destroyed if the serum samples are not properly stored and frozen before the assay. The present G-17 assay was initially set up to include a protein-rich drink 20 min before blood sampling. This protein stimulus doubles the G-17 levels in the serum, which improves the technical possibilities of measuring low G-17 levels immunochemically. However, the present study shows that the fasting S-G-17 levels are also applicable in the diagnosis of atrophic gastritis when cut-off levels are used for S-G-17_{fast} that are half of those for S-G-17_{prand}. When S-G-17_{fast} is applied, the sensitivity and specificity of the test panel are slightly lower than those by using the panel that applies S-G-17_{prand}.

Fasting and postprandial levels of S-G-17 are highly correlated, and the doubling of S-G-17 levels 20 min postprandially occurs in patients with initially low or high S-G-17_{fast} levels. This suggests indirectly that both fasting and postprandial S-G-17 levels reflect the number of G-cells in the antrum, i.e. protein stimulation may primarily empty the G-17 stores in the existing G-cells, and a peak in S-G-17 is seen 20 min after the stimulus. If the antral G-cells are numerous (as is often the case in the context of autoimmune corpus-limited atrophic gastritis in which the antrum is normal; non-atrophic), both fasting and postprandial S-G-17 levels are high, but if these cells are scarce (as in antral atrophy), both S-G-17 levels are low.

Diagnosis of atrophic gastritis by biopsy specimens is often unreliable, and the interobserver variation is large, in particular in antral biopsies [15]. This may be due to the fact that atrophic lesions are often patchy, and a limited number of biopsy specimens may easily result in under- or overdiagnosis. The existing inflammation may also bias the microscopic appearance and lead to overestimation of atrophic gastritis due to artificial impression of a loss of glands. It is conceivable that a blood test panel avoids these biases and will give an average estimate of the grade of atrophy and loss of normal glands and cells in the antrum and corpus. The present blood test panel is not capable, however, of detecting any local lesions or tiny focal patchy alterations in the gastric mucosa. Therefore, the blood test panel is not a direct test for cancer or peptic ulcer, but it may reveal patients who are at risk for these diseases and in whom endoscopy is mandatory.

In summary, our study shows that the blood test panel is a non-invasive alternative in the initial examination of patients with dyspepsia. In connection with the computer program GastroSoft, the panel seems to reliably and easily find patients with gastritis of various forms. In contrast to the testing of the *H. pylori* alone, the panel helps to identify easily and non-endoscopically patients with atrophic gastritis in the antrum or the corpus, or both, i.e. those in whom immediate endoscopy is necessary due to elevated cancer and ulcer risks, or in whom the treatment of *H. pylori* is strongly recommended due to major pathological alterations in the gastric mucosa and who are also at risk for deficiencies of vitamins or micronutrients due to advanced atrophic corpus gastritis.

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