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GastroPanel: the first non-invasive test for the diagnosis and classification of gastritis

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Abstract

GastroPanel® is the first-line diagnostic test for Helicobacter pylori (Hp) infection and for dyspepsia, and the screening test for atrophic gastritis (AG) with its associated risks such as cancer of the stomach and of the oesophagus. GastroPanel contains biomarkers including pepsinogen I (PGI), pepsinogen II (PGII), gastrin-17 (G-17) and anti-Helicobacter pylori antibodies. Enzyme immunoassay of their plasma levels provides precise information on the structure and the function of the gastric mucosa. GastroPanel is indicated to support the diagnosis of symptomatic (dyspeptic) and asymptomatic patients in order to detect the groups at risk of stomach cancer. GastroPanel is optimised through the use of the updated Sydney System (USS) for the classification of gastritis and of the GastroSoft® software. The results are classified as 1) normal mucosa, 2) superficial gastritis (Hp), 3) atrophic gastritis of the antrum, 4) atrophic gastritis of the corpus and 5) atrophic gastritis of the corpus and of the antrum (pangastritis).

GastroPanel is therefore the first non-invasive diagnostic test of the health of the gastric mucosa. It is unique in that the results are interpreted by a software application (GastroSoft) developed specifically for this purpose.

As a reminder

Gastrins are linear peptide hormones produced by the G cells of the duodenum, in the pyloric part of the antrum and in the pancreas. The main function of gastrins is to stimulate the secretion of gastric acid (HCl) by the parietal cells of the gastric corpus and to increase the motility of the antrum. In addition, gastrins are known to stimulate the secretion of pepsinogens (PGI, PGII) by the gastric chief cells and to induce the contraction of the lower oesophageal sphincter (LES). The G cells release into the circulation a mixture of gastrins of different molecular weights, including gastrin 71, 52, 34, 17, 14 and 6. In healthy human subjects, the dominant forms of gastrin in plasma/serum are gastrin 34 (G-34) and gastrin 17 (G-17). Gastrin G-17 is the predominant and most potent form in healthy antral tissue and is produced almost exclusively by the antral G cells. The G-17 included in this test is a direct biomarker of the structure and the function of the antrum and, through the negative feedback loop, an indirect biomarker of the gastric corpus. A plasma G-17 level within the normal range implies a normal structure and function of the antrum, whereas low or high G-17 values indicate a functional abnormality of the corpus.

Pepsinogen I (PGI) is a precursor (zymogen) of an enzyme, pepsin, synthesised by the chief cells and the neck cells of the corpus of the stomach (in the oxyntic glands). As a precursor of pepsin, most of the PGI is secreted into the gastric lumen, but a small part is also excreted into the blood. The concentration of circulating PGI is closely correlated with the number of chief cells in the mucosa of the corpus of the stomach, and any loss of these cells (due to atrophy of the mucosa) results in a linear reduction of the plasma PGI level.

Pepsinogen II (PGII) is produced by the chief cells and the mucous neck cells of the gastric corpus, in the pyloric glands of the antrum and in the Brunner's glands of the proximal duodenum. The plasma PGI/PGII ratio in normal subjects is approximately 3–20. The PGI/PGII ratio falls linearly as atrophic gastritis progresses in the corpus. This ratio drops below 3.0 when atrophic gastritis of the corpus is advanced (moderate or severe). It has been shown that the risk of stomach cancer increases (5-fold) when the PGI/PGII ratio is low. A raised PGII level indicates inflammation of the mucosa, the highest values being detected in non-atrophic gastritis associated with Hp. Since anti-Hp antibody levels may remain high for several months, even after eradication of Hp, PGII is a useful marker to confirm the success of the eradication.

Helicobacter pylori (H. pylori) infection is the main cause of chronic gastritis and causes atrophy of the mucosa. More rarely, AG may be caused by an autoimmune mechanism. H. pylori is a Gram-negative spiral bacterium that colonises the human stomach. This organism is found in the mucous layer covering the gastric epithelium and in the glands of the mucosa, but does not appear to invade the epithelial cells. However, the mucosa beneath and around the areas colonised by H. pylori is invariably inflamed. This condition, termed chronic superficial or non-atrophic gastritis, persists for life if left untreated. If the bacterium is not properly eradicated, this chronic inflammatory process causes atrophic gastritis.

Presentation of GastroPanel®

GastroPanel® is the first-line diagnostic test for Helicobacter pylori (Hp) infection, for the investigation of all patients suffering from dyspepsia, and for the screening of atrophic gastritis (AG) with associated risks such as cancer of the stomach and oesophagus. Atrophic gastritis increases the risk of malabsorption of vitamin B12, iron, magnesium, zinc, calcium and of certain drugs. GastroPanel contains key stomach-specific biomarkers representing the key regulators of normal gastric physiology. These four biomarkers are pepsinogen I (PGI), pepsinogen II (PGII), gastrin-17 (G-17) and anti-Hp antibodies; they are assayed by enzyme immunoassay and provide information on the structure and function of the gastric mucosa. This panel also gives a precise estimate of the capacity of the antral and corpus mucosa to secrete gastric acid, of the presence of significant gastric disorders such as inflammation, and finally of the level and topography of atrophic gastritis, which may represent an increased risk of stomach cancer. Normal plasma levels of the four biomarkers indicate that the gastric mucosa has a normal structure and function, whereas abnormal levels are signs of an unhealthy stomach and indicate abnormalities of the feedback mechanisms between acid secretion of the corpus, the PGs and G-17.

GastroPanel has been validated in several large-scale trials on biopsy-confirmed gastroscopies, all included in a meta-analysis on the subject. These studies established the validated reference (cut-off) values for each biomarker of the panel for each of the five histological indicators. They also confirm the high accuracy of GastroPanel for detecting the most important indicator, moderate to severe AG. Thus, normal values of PGI, PGII and their ratio (PGI/PGII) make it possible to rule out AG of the corpus with an NPV greater than 95%. Values of PGI and PGII and their ratio below the established cut-off levels indicate moderate to severe AG, with areas under the ROC curve (AUC) greater than 0.950 in series that are sufficiently powered and validated in the USS.

Good to know

Worldwide, stomach cancer remains the third leading cause of cancer death, and the achlorhydric stomach is the most important risk factor. According to a recent meta-analysis, chronic use of PPI drugs (proton pump inhibitors) is also associated with an increased risk of stomach cancer. The common cause of these two conditions is the carcinogenic (class I) acetaldehyde produced in the achlorhydric stomach. This information is very important, because identifying a specific carcinogenic substance makes it possible to take measures to reduce the exposure of the upper digestive tract to acetaldehyde, both at population and at individual level. To obtain this protection, all subjects with an achlorhydric stomach or AG of the corpus, and people who regularly take PPI drugs, are advised to use Acetium capsules to convert the carcinogenic acetaldehyde in the stomach into a harmless compound, thereby reducing the risk of cancer of the stomach and oesophagus.

The GastroPanel test can detect the following conditions:

1. H. pylori infection, which is an independent risk factor for stomach cancer and peptic ulcer.
2. H. pylori-induced atrophic gastritis (AG), asymptomatic in most cases, and the topographical site of the AG in the corpus and/or the antrum. Besides H. pylori, the other causes of AG developing in the corpus may also be an autoimmune mechanism.
3. AG in the corpus, which causes low acid secretion (achlorhydric stomach). This increases the risk of cancer of the stomach or oesophagus, as well as malabsorption of vitamin B 12, calcium, magnesium and zinc. Furthermore, the absorption of certain drugs such as dipyridamole, of certain iron preparations and of certain antifungals (fluconazole, itraconazole). The absorption of thyroxine and atazanovir is also compromised in the case of an achlorhydric stomach.
4. AG of the antrum, which increases the risk of peptic ulcer and stomach cancer. The coexistence of AG of the corpus and of the antrum is the dominant risk factor for stomach cancer.
5. H. pylori infection, also in subjects with AG, a MALT-type lymphoma or a haemorrhagic peptic ulcer, or when PPI drugs or antibiotics are being taken. In these cases, C13-labelled urea breath tests or the search for Hp antigens in stool often give false negative results, and H. pylori infection (and all its consequences) is not detected.
6. High acid secretion of the gastric mucosa, which predisposes to oesophageal reflux and its potential complications (ulcerative oesophagitis, Barrett's oesophagus or cancer of the lower oesophagus). AG, high acid secretion and symptomatic H. pylori infection are indications for gastroscopy.

Conclusion

GastroPanel appears as an innovative tool in the management of gastritis. It is relatively inexpensive, non-invasive and accessible. Laboratoire Sion makes this panel available to any physician who needs it for better patient management. This test remains the best tool in the management of gastritis and is also the ideal complement to gastroscopy.

Table 1: Proposed scheme for the management of gastritis after classification by GastroPanel

	Gastric condition	Management of the gastritis
01	Healthy mucosa. High acid secretion in the corpus	PPI
02	Healthy mucosa. Low acid secretion. Due for example to the intake of PPI drugs	1. Ulcar (sucrafate) 1 g: 1 sachet x 2/day for 30 days 2. Acetium 100 mg: 1 capsule x 2/day for 30 days 3. NB, advise taking lemon
03	H. pylori infection, no atrophy	1. First line: triple therapy 2x/day for 14 days, PPI, clarithromycin (500) + metronidazole (500) or amoxicillin (1000) 2. Second line: Quadruple Therapies for 14 days; Furazolidone 200 mg, Colloidal Bismuth Subcitrate (DeNol) 120 mg, Amoxicillin 1000 mg, and PPI. 3. Third line: Quadruple therapies "rescue therapy" for 14 days: Ciprofloxacin 500 mg, Rifabutin 150 mg, Omeprazole 40 mg, Amoxycillin 1000 mg.
04	Gastric inflammation (H. pylori negative). Due for example to the intake of drugs, alcohol, bile reflux	1. Misoprostol 75 mg 2. Ulcar (sucralfate) 1 g for 14–20 days
05	Atrophic gastritis of the corpus, due to H. pylori infection	1. Treat the H. pylori infection without PPI, for 14 days plus 2. Ulcar (sucralfate) 1 g for 30–45 days or more 3. Vitamin B12 amp (IM): 3x/week for at least 8 weeks 4. Acetium 100 mg for 30–45 days
06	Atrophic gastritis of the corpus (t) Due to autoimmune causes	1. Treat the H. pylori infection; triple therapies, for 14 days plus 2. Ulcar (sucralfate) 1 g for 30–45 days plus 3. Acetium 100 mg for 30–45 days
07	Atrophic gastritis of the antrum and of the corpus	1. Treat the H pylori infection without PPI, for 14 days plus 2. Ulcar (sucralfate) 1 g for 30–45 days plus 3. Vitamin B12 amp (IM): 3x/week for at least 8 weeks 4. Acetium 100 mg for 30–45 days

Biographies

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