Reprint from: **Yksityislääkäri-lehti 5/06 (2006)(www.google.com/Hyvä Kollega 2006);** GastroPanel for the development of a safe management and treatment practice for dyspepsia, *Helicobacter pylori* infection and atrophic gastritis with related risks.

Dear Colleague

- As to the inquiries by many colleagues regarding to the benefits and costs of GastroPanel testing as compared with the current practice, I would propose the following. Although the use of GastroPanel from a blood sample is also increasing In Finland, a two-stage strategy is recommended for the diagnosis and treatment of dyspepsia and Helicobacter pylori infection, using “test and treat” strategy and test treatment with proton pump inhibitors (PPI). According to this recommendation, *Helicobacter pylori* is examined primarily by a breath test or secondarily by fecal antigen test (In Table, 13C-urea breath test, UBT or stool antigen test, SAT). If the result is positive, the patient receives eradication treatment and the response to treatment is controlled. PPI medication is being tested in a *Helicobacter pylori*-negative patient. This recommendation, heavily marketed in Finland by the Swedish listed company Orexo AB (Diabact UBT) (1,2) is not safe.

Serious medical and ethical issues associated to the breath test and stool antigen test

- UBT and SAT tests give up to 40-50% false negative results if the patient has a) atrophic gastritis, b) MALT lymphoma or c) bleeding peptic ulcer disease, or d) if the patient is currently being treated with antibiotics or PPI medication (3 - 6).

  UBT and SAT tests give false negative results precisely in cases where the patient’s *Helicobacter pylori infection* should be found and treated, e.g. because of increased gastric cancer risk associated with atrophic gastritis. UBT and SAT tests do not detect atrophic gastritis, which is particularly important to detect, because this lesion may be on the way to gastric cancer. Therefore, each *Helicobacter pylori* positive person with atrophic gastritis should be referred for gastroscopy and appropriate treatment. Even if *Helicobacter pylori* eradication treatment with antibiotics and PPIs would be successful, the more advanced precursors of cancer (intestinal metaplasia, dysplasia) have been found to progress to gastric cancer.

  Recent follow-up studies on the role of *Helicobacter pylori* eradication therapy in preventing gastric cancer have been disappointing but have provided significant new information. It turns out that eradication treatment does not prevent cancer in patients with advanced atrophic gastritis (and coexistent cancer precursor lesion - dysplasia). In contrast, eradication therapy appears to be effective in patients who do not yet have atrophic gastritis. These findings underline the importance of diagnosing atrophic gastritis when eradication therapy is considered as a cancer prevention. Patients with atrophic gastritis should be referred for gastroscopy (to disclose and treat eventual cancer precursors), whereas patients with non-atrophic gastritis are likely to be safely eradicated without endoscopy (Sipponen and Graham 2006, Kuipers and Sipponen 2006).

  A study is ongoing at HUS (Helsinki University Hospital) to find out e.g. in how many patients with gastric cancer have been diagnosed (apparently only by UBT) and treated for a *Helicobacter pylori* infection before the onset of cancer. Preliminary data from this study suggest that eradication therapy has been given to a significant proportion of gastric cancer patients a few years before the cancer was diagnosed. Eradication therapy has apparently not prevented the development of cancer in patients who have had advanced atrophic gastritis at the time of the eradication therapy, possibly with coexisting cancer precursor (or “early cancer”).

The same has been confirmed recently in China by the so called "Wong-study". Similarly, the study of Professor Timo Kosunen (recently published as an abstract), conducted on patients receiving eradication therapy in Finland, also shows that new cases of gastric cancer appear even several years after a successful eradication therapy.

- An interesting case reported by Dr Leena Järvinen (an occupational health specialist) is an example implicating that a successful eradication therapy may lead to a slow, protracted recovery of an early atrophic gastritis, if *Helicobacter pylori* infection and the associated atrophic gastritis are correctly diagnosed on time (17). In the management of this dyspeptic patients, the initially followed two-step strategy failed to disclose *Helicobacter pylori* infection by the UBT test, and the instituted PPI test treatment did not improve the patient's symptoms (in fact, the patient's stomach was almost acid-free!). Even the subsequent gastroscopy detected anything else but a moderate atrophic gastritis of the corpus, and therefore, the patient was diagnosed with corpus atrophy of the autoimmune-type. Afterwards, the patient coincidentally searched for GastroPanel examination, where *Helicobacter pylori* infection and severe atrophic gastritis of the corpus were disclosed. The patient received eradication therapy, and subsequently gastric atrophy has shown signs of healing both in GastroPanel and histological examinations.

  A number of similar cases exist, one being a 67-year-old woman who has suffered from dyspeptic symptoms for years. On gastroscopy performed in December 2004 and October 2005, gastric mucosa was considered healthy (no atrophy). The patient has used PPI medication for a long time. In August 2006, a carefully performed gastroscopy revealed chronic atrophic corpus gastritis. This diagnosis was confirmed by GastroPanel, detecting moderate atrophic corpus gastritis in September 2006. Similar as the previous case, also this patient had received long-term PPI medication, despite the fact that she had acid-free stomach due to corpus atrophy. For the patients with atrophic corpus gastritis, PPI test treatment or even worse, prolonged PPI treatment can be even fatal e.g. because of the possibility for delayed diagnosis and treatment of potentially curable gastric cancer precursors (atrophic gastritis, intestinal metaplasia and dysplasia).

  According to Docent Anna-Liisa Karvonen (specialized gastroenterologist), it can be estimated that in Finland, some 200 - 300 people are dying every year from a bleeding gastro-duodenal ulcer and its sequels (Karvonen AL. Vatsavaivaa – Milloin tutkimuksiin, Mehiläinen, Terveydenhuoltoa. Yksityisesti, 3 – 2006, pp. 8- 9).

  Gastric or duodenal ulcer disease (peptic ulcer disease) is most often caused by *Helicobacter pylori* infection. As presented above, UBT and SAT test frequently fail to find *Helicobacter pylori* infection. Similarly, these *Helicobacter pylori* tests do not provide information on e.g. atrophic antrum gastritis, which together with *Helicobacter pylori* infection, substantially increases the risk of peptic ulcer disease. Because of this, the risk, cause and diagnosis of peptic ulcer disease may remain undisclosed, which may be a major reason for the above-mentioned bleeding deaths, in connection with NSAIDs.

Prof. Barry Marshall and Prof. Osmo Suovaniemi at the exhibition stand of GastroPanel during the 50th anniversary meeting of the Finnish Gastroenterology Association, Turku September 7-8, 2006. GastroPanel has a link to the 2005 Nobel Prize, through the gastric inflammation by *Helicobacter pylori* infection (gastritis), which can progress to atrophic gastritis. Both Nobel laureates, Professors Robin Warren and Barry Marshall, have been involved in a basic research during the development of GastroPanel.

- It would be worth assessing, e.g. how many of these deaths could be prevented by using GastroPanel; its serological *Helicobacter pylori* test for IgA & IgG antibodies reliably detects *Helicobacter pylori* infection (3 - 6) and other GastroPanel biomarkers diagnose atrophic gastritis and associated risks (www.gastropanel.com):

  1. Pepsinogen I (PG I) and the PGI/PGII ratio indicate atrophic gastritis of the corpus mucosa (glandular loss and consequent dysfunction), its severity increasing with the lower biomarker values. Atrophic corpus gastritis poses a risk of gastric cancer and vitamin-B12 deficiency. Vitamin-B12 deficiency can lead to dementia, depression and polyneuropathy, as well as to high levels of homocysteine, which in turn is believed to be an independent risk factor for atherosclerosis with cerebrovascular- and cardiac thrombosis.

  2. If a patient has atrophic corpus gastritis or is a chronic user of taking PPI medication, the stomach is hypoacidic or acid-free ("no acid no wound"). However, a hypoacidic stomach is associated with a markedly increased risk of gastric cancer. In addition, in a hypoacidic stomach, oral bacteria colonize and produce carcinogenic acetaldehyde from food-derived carbohydrates.

  3. Gastrin-17 indicates atrophic gastritis of the gastric antrum, severity of which being correlate with progressively declining gastrin-17 levels. If a patient has *Helicobacter pylor*i infection and low gastrin-17, the risk of gastric cancer and peptic ulcer disease is significantly increased.

  4. In the absence of *Helicobacter pylori* infection, low gastrin-17 indicates high acid (HCl) output of the corpus, which may cause severe complications of esophageal reflux disease (erosive esophagitis and Barrett's esophagus). An increased acid output of the corpus is also associated with elevated PG I levels.

GastroPanel saves the costs of the healthcare, employers and patients and improves general well-being

- Examinations included in the two-stage screening strategy for the diagnosis of dyspepsia (1,2) result in significant costs, not to mention the many-fold higher costs and human suffering caused by the lack of care or by the treatment instituted without diagnosis or on the basis of a misdiagnosis. The cost of a UBT test in a private laboratory equals to € 72.00 (in 2006). A four-week PPI test treatment costs € 61.60. Other examinations involved in the two-step strategy include an ESR (€ 9.90), a low blood count (€ 21.40), ALAT (€ 16.90), a lactose intolerance gene test (€ 54.10 €), celiac panel (€ 56.20) and fecal occult blood (€ 23.00). The total cost of these tests equal to € 315.10.

  None of the above tests included in the two-step screening strategy provides any information on the function of the gastric mucosa in a dyspeptic patient, or the mucosal status, i.e., is the mucosa actually healthy or affected. The UBT or SAT test does not make this significant distinction. Patient with a negative UBT, may present with a significant gastric pathology. A negative UBT is not infrequent in patients with severe atrophic gastritis - the disease with the highest risk of gastric cancer. Atrophic gastritis with the potential associated risks (gastric cancer, vitamin-B12 deficiency and peptic ulcer disease) as well as the complications of esophageal reflux disease can only be diagnosed using gastroscopy and GastroPanel examination.

  In many cases, GastroPanel testing could replace all or part of the above examination in the fist-line diagnosis. In addition, GastroPanel test distinguishes between functional and organic

dyspepsia (see Table), thus sparing up to over 50% of all dyspeptic patients from unnecessary gastroscopies (about € 300 / one gastroscopy). GastroPanel helps targeting the insufficient and expensive endoscopy resources more accurately and effectively.

The Social Insurance Institution of Finland (KELA) reimburses GastroPanel test

- KELA reimburses approximately € 60 for GastroPanel tests performed on a doctor's prescription. Private laboratories charge the GastroPanel tests (pepsinogen I and pepsinogen II and gastrin-17 and H. pylori antibodies) around 120 €. - If Biohit service laboratory performs the GastroPanel test, it will charge the health center a total of € 70 for a GastroPanel test and the GastroSoft report (www.biohit.fi / Palvelulaboratorio).

Costs associated with GastroPanel testing in health centers and hospitals

- If the GastroPanel test is performed in-house at a health center or hospital, the reagents for a test (all four biomarkers) will cost about € 30. For the completion of the GastroPanel test, Biohit supplies both the reagents and the equipment, unless microplate readers, washers and pipettes are already in use in the laboratory (total cost of about € 10,000; can also be leased).

The GastroPanel innovation and the fundamental basic research in Finland together with the *Helicobacter pylori* discovery - A major step forward in medicine

- Australian physicians Barry J. Marshall and J. Robin Warren received the 2005 Nobel Prize in Medicine, due to their discovery in 1982 implicating that *Helicobacter pylori* infection causes gastritis and peptic ulcer disease (http://nobelprize.org/medicine/laureates/2005/press.html). The benefit obtainable in medical practice from this discovery is greatly increased with the invention of GastroPanel. These two innovations together contribute to the development of more safe and more cost-effective diagnostic and management practices.

  The serious medical and ethical problems of the “test and treat” strategy can be circumvented simply and cost-effectively by replacing the UBT (and SAT) tests used in this strategy by the GastroPanel test, which provides a wealth of information to support the diagnosis and treatment (see Table).

  The GastroSoft software application used to interpret the GastroPanel test results, is based on extensive clinical trials where patients have been examined with GastroPanel and gastroscopy (see Table, www.gastropanel.com).

  Accordingly, GastroPanel is a safe and cost-effective means to diagnose dyspepsia, *Helicobacter pylori* infection and atrophic gastritis, with all its associated risks. Due to its ease of use, GastroPanel is also suitable for the population-based screening to identify and timely treat the patients at increased risk for gastric cancer. With GastroPanel screening, approximately 75% of gastric cancers are detected at an early stage when amenable to surgical or endoscopic curative therapy. In the current clinical practice, this percentage is below 20%. In addition to the risk of gastric cancer, atrophic gastritis presenting with non-specific symptoms or most often asymptomatic, can cause peptic ulcer disease and vitamin- B12 deficiency.

GastroPanel detects the risk of vitamin-B12 deficiency- an emerging disease burden in the aging population

- Studies by Sipponen et al. have revealed a disease that seems to affect up to 10% of elderly people in Finland. This disease is a deficiency of vitamin-B12 due to undiagnosed atrophic gastritis of the stomach corpus. As a result of atrophic gastritis, the secretion of so-called intrinsic factor is reduced so that vitamin-B12 in the foodstuffs is not absorbed and the person suffers from vitamin deficiency. Vitamin-B12 deficiency has been considered to be related to e.g. dementia, depression and peripheral neuropathy (www.b12.com). Vitamin-B12 deficiency also results in increase in homocysteine concentration in the body, which is thought to be an independent risk factor for atherosclerosis, with cardiovascular and cerebrovascular thrombosis.

  Vitamin B12 deficiency and its causes are curable, if these persons can be identified, which is often not the case at present. One can only speculate how much of the disease burden could be prevented or alleviated, if the senior citizens exposed to vitamin-B12 deficiency due to atrophic corpus gastritis (few patients are under 50 years) are found by GastroPanel or gastroscopy and treated properly.

Table

At an early stage	The stochastic GastroSoft report states:	^{13}C - urea breath test or Stool antigen testreport:
The diagnosis for		
Functional vs. organic dyspepsia. When GastroPanel indicates the gastric mucosa is healthy, the dyspepsia complaints are often caused by functional dyspepsia or another disease not involving the gastric mucosa	YES	NO
***H. pylori* infection** (gastritis)	YES	NOT RELIABLE (1)
Atrophic gastritis (damaged and severely dysfunctional gastric mucosa) and the probabilities of different conditions affecting the mucosa of the gastric corpus or antrum or both (normal, gastritis or atrophic gastritis)	YES	NO
The risks (related to atrophic gastritis) of		
Gastric cancer	YES	YES/NO (2)
Vitamin B12 deficiency	YES	NO
Peptic ulcer disease	YES	YES/NO (3)
The risks of the complications of		
Gastroesophageal reflux disease: **Esophagitis and Barrett's esophagus**	YES (4)	NO
If necessary, a recommendation for		
Gastroscopy and biopsy examination	YES	NO
Treatment of *H. pylori* infection	YES	YES/NO (5)
Determination of vitamin B12 and homocysteine	YES	NO
Follow-up examination to monitor		
the incidence of atrophic gastritis	YES	NO
the healing of the *H. pylori* infection	YES	YES
the healing of atrophic gastritis	YES	NO

1) The 13C- urea breath - and stool antigen tests give false negative results if the patient has a) atrophic gastritis (a risk of gastric cancer and peptic ulcer disease and vitamin B12 deficiency and related diseases, such as dementia, depression and polyneuropathies as well as atherosclerosis, strokes and heart attacks) or b) MALT lymphoma or c) bleeding peptic ulcer disease or d) if the patient is currently receiving Antibiotics or PPIs (proton pump inhibitors).

(2) The risk of gastric cancer is very low without atrophic gastritis in the corpus, antrum or both. but in some cases, a H. pylori infection without histologically observable atrophic gastritis may be associated with gastric cancer and peptic ulcer disease.

(3) No peptic ulcer disease with Corpus atrophy (no acid, no ulcer). The risk of peptic ulcer disease is very low without antrum atrophy.

(4) High pepsinogen I (over 120 ug / l) and high pepsinogen I and II ratio (over 10) and low gastrin-17 (below 2 umol / l) indicate high acid (HCl) output and risks for the complications of gastroesophageal reflux disease.

(5) When the incidence of H. pylori -related atrophic gastritis is monitored, the patient may be offered targeted, safe treatment at the right time. The need for medication and the costs and adverse effects of medication can thus be reduced. If the patient has been diagnosed with peptic ulcer disease (gastric or duodenal ulcer), the H. pylori infection has to be treated (6). It should also be treated if the patient has atrophic gastritis. The patient and the doctor may also agree on eradication treatment for other reasons for example when the patient's close relatives have been diagnosed with gastric cancer.

(6) Press Release: The 2005 Nobel Prize in Physiology or Medicine, 3 October 2005 jointly to Barry Marshall and J. Robin Warren for their Discovery of "the bacterium Helicobacter pylori and its role in gastritis and peptic ulcer disease ": -" An indiscriminate use of Antibiotics to eradicate Helicobacter pylori also from healthy carriers would lead to severe problems with bacterial resistance against these important drugs. Therefore, treatment against

Helicobacter pylori should be used restrictively in patients without documented gastric or duodenal ulcer disease. ” http://nobelprize.org/medicine/ laureates / 2005 / press.html
Sipponen P, Jauhonen P, Suovaniemi O. GastroPanel for dyspepsia, Helicobacter pylori infection and atrophic the development of safe research and treatment practices for gastritis and related risks. Yksityislääkäri 2005; 6: 95-98 (see www, biohit.com/Diagnostics/Literature).

GastroPanel - for the benefit of general practitioners and different specialists

- The diagnostic information obtained from GastroPanel (see table) benefits in particular the physicians in health centers and occupational health sector, because GastroPanel is particularly intended for those forefront medical staff. As stipulated above, GastroPanel would be useful for many specialists as well, including the psychiatrist contemplating the origins of dementia as well as a neurologist assessing the causes of a cerebral infarction. It would not harm even if a cardiologist would take into account of what are the known consequences of corpus atrophy. A patient with peptic ulcer consulting surgeon or internal medicine specialist most often has *Helicobacter pylori* infection andassociated atrophic antrum gastritis, with a potential to progress to gastric cancer.

  For gastroenterologists, GastroPanel refers more patients who are in urgent need of gastroscopy. In addition to this, the gastroenterologist obtains the information from a GastroPanel test, implicating e.g. the potential site (corpus or antrum or both) where atrophic gastritis is likely to locate and what eventual risks the patient might have. Without a prior GastroPanel examination, the gastroscopist must rely on correctly targeted biopsies and their correct interpretation by the pathologist, if he wants to reach a correct diagnosis of the gastric mucosal status and function.

  Gastroscopy following GastroPanel examination should be combined with lactose intolerance *and Helicobacter pylori* testing in the biopsy specimens (Biohit H. pylori- and hypolactasia quick tests; Kuokkanen et al. 2006). With this practice, gastroscopic examination provides more information about the patient with dyspeptic symptoms, and in addition, the procedure minimizes the discomfort for the patient and saves healthcare costs.

Professors Pelayo Correa from the USA, Shu-Dong Xiao and Pentti Sipponen from Finland. "Gastritis Consensus Workshop " led by Professor Xiao in Shanghai on September 15-16, 2006 decided to implement GastroPanel in the Chinese healthcare.

Is GastroPanel a necessary routine test adjunct to those already used in health monitoring of people above 45 years?

- This question might have been already answered above and in the following. In a multicenter study of 43-73-year-old patients in Finland, 404 dyspeptic patients referred for gastroscopy according to routine practice, were also subjected to GastroPanel examination. Both tests were concordant in that more than half of the subjects had a healthy stomach, while approximately 12% of the subjects had moderate to severe atrophic gastritis in the corpus, antrum or both, indicating immediate gastroscopy. When fasting blood samples were used in the GastroPanel test, the concordance with gastroscopy was 81% (77-85%)(Väänänen et al. 2003).

  However, when comparing the GastroPanel and gastroscopy diagnosis of atrophic gastritis, it should be noted that reaching the correct diagnosis in a few biopsy specimens is not always possible, and it is not uncommon that two different pathologists end up with different diagnoses in the same patient. The quality of the results thus depends very much on the competence and diligence of the gastroenterologist and pathologist. These problems are not related to the GastroPanel test, which is based on biomarkers measured from a blood sample independently of the investigators, provide objective information on the structure and function of the gastric mucosa. If alarming changes in the biomarker levels are found, the patient should be further examined by careful gastroscopy, in which the information provided by GastroPanel is of great assistance (Väänänen et al. 2003, Rugge et al. 2002).

  The Finnish Setti study enrolled 23,000 male smokers aged 50–65 (6). Based on the results of the study, it was estimated that 250 to 300 gastric cancer deaths among the patients over 50 years could likely to be prevented annually in Finland. This is possible by screening for atrophic gastritis and its associated risks of gastric cancer by using GastroPanel examination, followed by gastroscopy to all those with atrophic gastritis. It is possible that the majority of cancers detected by this screening are early stage cancers for which surgical treatment is curative.

  However, it must be remembered that GastroPanel helps find (for referral to gastroscopy and treatment) only those patients at risk for gastric cancer whose gastric cancer progresses through atrophic gastritis. A proportion of gastric cancers develops without histologically detectable atrophic gastritis, and a small proportion of gastric cancers are also hereditary. It remains to be seen, e.g.. whether GastroPanel biomarkers are helpful in identifying the risks of these cancers and in the treatment of the patients at risk (more examples on research topics: www.biohithealthcare.com /Scientific/Study protocols, www.gastropanel.com).

  A large endoscopy follow-up study in England with over 10 years of follow-up, it was found e.g. that atrophic gastritis and subsequent intestinal metaplasia were associated with an 11% risk of stomach cancer (7). Gastric cancer is believed develop through stepwise process with several stages (Correa Cascade of gastric Carcinogenesis, 18)(8 - 11).

  In her article in the Finnish Medical Journal, Dr. Anna-Liisa Karvonen (specialized gastroenterologist, MD, Docent) states that GastroPanel is suitable for the risk assessment of asymptomatic patients when the primary goal is an early diagnosis of gastric cancer i.e., in the screening for gastroscopy of the patients with atrophic gastritis (12).

  Because atrophic gastritis is presented with non-specific symptoms or is usually asymptomatic, GastroPanel as a routine test for all abdominal symptoms, and for all those over 45 years of age increases the patient safety and reduces healthcare costs.

  GastroPanel test promotes the development of studies screening the risk of both peptic ulcer disease and esophageal reflux disease and their complications (13). GastroPanel is also useful in screening for the risk of vitamin-B12 deficiency (14). GastroPanel is cost-effective e.g.

because it provides evidence on the high-prevalence diseases and their related risks. In the world population, dyspepsia is present in 20-40%, *Helicobacter pylori* infection on average in over 50%, atrophic gastritis in up to 25%, peptic ulcer disease in 5-10%, vitamin-B12 deficiency (particularly among those aging 60 and above) in 10% or more, and gastric cancer in 0.1 to 1.0% or even more in some geographic areas. Esophageal reflux disease affects on average some 25% of the population.

Global evaluation of GastroPanel, its approvals and spreading use

- During the past few years, the applicability of GastroPanel has already been studied in approximately 40,000 patients around the world. GastroPanel has a marketing authorization for clinical use, e.g. in all EU countries, Russia, Ukraine, China and Canada. In the US, an application for FDA approval has been submitted, and the required additional studies ongoing, and a similar procedure in Japan is in progress.

  Introduction of the GastroPanel test in the primary diagnosis of dyspepsia, *Helicobacter pylori* infection and atrophic gastritis is underway around the world. Many service laboratories already offer GastroPanel tets. The world's largest service laboratory, the American Quest Diagnostics, has taken GastroPanel in its repertoire in the UK over a year ago. Leading Italian gastroenterology experts wrote a guide on GastroPanel test use (DiMario et al. 2004), which was distributed to over 35.000 general practitioners in Italy by AstraZeneca, the world's marker leader of PPIs. The aim of this guide is to introduce GastroPanel test to all people suffering from dyspepsia-type symptoms in the primary health care. GastroPanel test, together with the anamnestic data and clinical examinations help refer the dyspeptic patient to possible further examinations on the correct basis, and ultimately lead to correct diagnosis and proper treatment (www.biohit.com/Diagnostics/Literature).

  In Shanghai, the top health experts and opinion leaders of China hosted in September 15-16, 2006, The "Gastritis Consensus Workshop", chaired by Professor Shu-Dong Xiao. Altogether, 67 lecturers and other participants from across China had been invited to the workshop. As the only foreign experts invited to the Workshop were the pioneers in this field: Professor Pelayo Correa (Correa cascade of carcinogenesis, 18) and Professor Pentti Sipponen from Finland (atrophic gastritis, gastric cancer). Professors Xiao, Correa and Sipponen as well as other Chinese professors addressed in their lectures the use of GastroPanel and the benefits of the test. Already before, GastroPanel has received an import license to China, and the above-mentioned working group decided to implement GastroPanel test in the national healthcare in China.

GastroPanel increases the targeted use of endoscopy resources and PPI medications

- In the discussions held in Shanghai on 15-16 September, 2006, Professor Correa emphasized e.g. that the use of GastroPanel does not reduce the need for gastroscopies, but on the contrary, it targets them correctly to the patients in real need. In addition, GastroPanel testing increases the need for gastroscopies because it finds more often and more reliably than the UBT test, *Helicobacter pylori* infection and, in addition, atrophic gastritis due to *Helicobacter pylori* infection (rarely autoimmune disease) and associated risks (atrophic corpus gastritis: gastric cancer and vitamin-B12 deficiency; atrophic antrum gastritis: gastric cancer and peptic ulcer disease). The atrophic gastritis detected by GastroPanel necessitates gastroscopy and appropriate treatment based on the results.

  GastroPanel often finds the risks of complications of esophageal reflux disease that require gastroscopic confirmation also in asymptomatic people (about a third of patients with reflux disease are asymptomatic – even if the reflux disease has already led to severe esophagitis and Barrett's esophagus). GastroPanel increases the correct and ethical use of PPI, which the pharmaceutical companies are striving to. Accordingly, also the PPI manufacturers and the patients benefit from GastroPanel test.

Updating the Finnish national management guidelines with GastroPanel

- A working group set up by the Finnish Gastroenterology Association has launched the national guidelines on the diagnosis and treatment of *Helicobacter pylori* infection in 2002, when GastroPanel was not yet widely known in Finland. At present, when GastroPanel has been evaluated and tested all over the world, there is probably no obstacle to accept GastroPanel in Finland into the management guidelines on treatment of *Helicobacter pylori* infection as an integral part of the "test and treat" strategy. That would promote the evidence-based care, which is not the case with the current management guidelines with the "test and treat" strategy (15,16). An update of these management guidelines can reduce unnecessary examinations, delayed treatment times, human sufferings and healthcare costs.

  While awaiting an update of the current management guidelines, each physician now has an opportunity to make his or her own judgment to avoid the above listed serious medical and ethical problems, for which the 2002 management guidelines do not pose obstacles - on the contrary, it suggests the best possible diagnosis and treatment (see the working group "Limitation of Liability"). Over one million Finnish citizens suffering from dyspepsia-type upper abdominal symptoms are entitled to implementation of novel and more safe examination methods. This can be realized simply and in a cost-saving manner by using GastroPanel testing. This will support the correct diagnosis and appropriate treatment, is highly informative and a readily applicable tool as a part of the 'test and treat' strategy for diagnosis of *Helicobacter pylori* infection, instead of the obsolete UBT and SAT tests (see table).

"Limitation of liability

- Current management guidelines are summaries by the best experts on the diagnosis of individual diseases and on the impact of their treatment. They are not a substitute for personal judgement of your own doctor or other healthcare professional evaluating the optimal diagnostic strategy and treatment of the individual patient while making treatment decisions."

The European Helicobacter pylori Study Group

- The chairman of the 2005 meeting of the European Helicobacter Pylori Study Group (Maastricht 3-2005, of which no official report has been published yet) Professor Peter Malfertheiner informed this author a few months ago that the value of the serological *Helicobacter* test is recognized and the limitations of the UBT (and also the SAT) tests are well known. Prof. Malfertheiner also told that despite this, the breath test (UBT) is still widely used and recommended because of its marketing and sales by various parties is still very aggressive, including generous rewards to opinion leaders and consultants. According to Prof. Malfertheiner, the "test and treat" strategy could now be further improved by replacing the UBT (and SAT) tests with GastroPanel.

Barry Marshall, the Laureate of the 2005 Nobel Prize in Medicine highly appreciates gastritis research in Finland

- Professor Marshall highly appreciates the scientific work of Professor Max Siurala's Finnish-Estonian research group and the pioneering work of their partner Professor Pentti Sipponen, which in part, paved the way to the Nobel Prize-winning invention of 1982 made by him and his colleague Professor Robin Warren's (http://nobelprize.org/medicine/ laureates/ 2005/press.html). The GastroPanel innovation complements these achievements and enables their more effective utilization in practical medicine (www.gastropanel.net). Naturally, Barry Marshall hopes that this work will continue and its results could be exploited in the development of medicine in Finland as well. Prof. Barry Marshall was awarded the Max-Siurala price at the

annual meeting of gastroenterologists (Finnish Gastroenterology Association: the 50th anniversary meeting held at the Turku Fair and Congress Center on 7-8 September 2006. Theme: “Gastroenterology achievements and future prospects ”).

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3. In the two-stage screening method, the 13C urea breath test is recommended as the primary test for detecting Helicobacter pylori infections. This
test is nevertheless only reliable when Helicobacter pylori infection is fresh and the number of bacteria is high. Its sensitivity decreases significantly if the
number of bacteria is small. For this reason, the 13C urea breath test gives false negative results in more than 50% of patients with Helicobacter pylori
infection and severe atrophic gastritis of the stomach mucosa (Kokkola et al., 1998, 2002). If the patient is on PPI medication, the 13C urea breath test
gives a false negative result in almost 40% of cases. Bismuth-containing medicines and antibiotics further increase the number of false results. In these
cases, too, a serological antibody test gives more reliable results than the 13C urea breath test (Graham et al. 2002, 2003, Gatta et al. 2004). The 13C
urea breath test alone does not detect atrophic gastritis, and in addition, the false negative result means that the Helicobacter pylori infection and therefore
also the atrophic gastritis are left untreated. These problems do not occur when the Helicobacter pylori test is performed using a serological antibody
test (Kokkola et al. 1998, 2002), particularly when GastroPanel, in addition to its serological IgG&IgA H. pylori antibody test, includes biomarkers
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