Additional information

Acetium® and GastroPanel® inventions: The GastroPanel® blood examination reveals, e.g., atrophic gastritis (anacidic stomach) with related risks, such as risk of stomach and oesophageal cancer. Acetium® capsules, that bind the carcinogenic acetaldehyde in stomach, may decrease i.e. the risk of these serious cancers.

The GastroPanel® and Acetium® innovations are together a unique combination that can help to prevent gastric and oesophageal cancers. GastroPanel® detects atrophic gastritis and the related gastric and oesophageal cancer risks while the conditions are still treatable. Atrophic gastritis of the corpus, which is usually irreversible, leads to permanent achlorhydria. In an achlorhydric stomach (also caused by a long term PPI-treatment), microbes from the mouth can survive and produce acetaldehyde from sugars and alcohol present in food. In the new cancer classification issued by WHO in October 2009, acetaldehyde present in alcoholic beverages and formed from ethanol endogenously is in Group 1, together with carcinogens such as asbestos, tobacco and benzene. Globally, acetaldehyde exposure mediated by gastrointestinal tract microbes or tobacco smoke is associated with approximately four million new cases of cancer each year, nearly 40 per cent of all cancers. These include upper aerodigestive tract, colon and pulmonary cancers. Biohit has developed Acetium® products and a method to reduce physical and nutritional exposure to acetaldehyde (www.biohithealthcare.com/scientific/study-protocols).

The state-of-the-art, safe and economic GastroPanel® examination for the diagnosis of *Helicobacter pylori* (*H.pylori*) infection and atrophic gastritis does not have any of the following serious medical problems:

The ^{13}C urea breath test (UBT), stool antigen test and antibody tests for *H. pylori* infection do not detect atrophic gastritis which is caused by *H. pylori* infection or an autoimmune disease. The early and reliable diagnosis of atrophic gastritis is important and often life-saving because of its several risks, including, e.g., unnecessary deaths due to stomach and oesophageal cancer.

In addition to the risks of gastric and oesophageal cancer, atrophic gastritis may cause malabsorption of vitamin B12, iron, magnesium, calcium and some drugs. Calcium deficiency causes osteoporosis, and vitamin B12 deficiency can cause Alzheimer's disease, dementia, depression and polyneuropathy, as well as high homocysteine content in the body, which in turn is thought to be an independent risk factor for atherosclerosis, heart attacks and strokes. The absorption of dipyridamole, some iron products and antifungals (fluconazole, itraconazole), thyroxine and atazanavir is considerably impaired in an anacidic stomach.

Atrophic gastritis in the gastric corpus and PPI therapy cause anacidity (aclorhydria) of the stomach. The risk of pneumonias and, in senior citizens, even the risk of fatal intestinal infections (such as giardiasis, malaria, *Clostridium difficile* and *E. coli* EHEC) may increase significantly in an anacidic stomach.

H. pylori gastritis may i.e. also develop into antral atrophic gastritis, which increases the risk of peptic ulcer disease and gastric cancer. If both antrum and corpus mucosa are atrophic, this condition is the highest risk for gastric cancer known to date.

Furthermore, none of the aforementioned three *H. pylori* tests (^{13}C urea breath test, stool antigen test and antibody test) provides any information on excessive gastric acid secretion (high acid output), which in patients with gastro-oesophageal reflux disease may cause complications of this disease in esophagus. Such complications are often asymptomatic and include ulcerative oesophagitis and Barrett's oesophagus, which

may lead to oesophageal cancer if left untreated. In addition, the 13C urea breath test and stool antigen test may give up to 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 receiving antibiotics or PPIs.

The GastroPanel® examination arguments for general practitioners – for huge unmet need (indications)

- GastroPanel® should be the first-line diagnostic test for the diagnosis of *H. pylori* infection (5-80% of the world population) and in examination of all patients with dyspepsia (20-40% of the western population).
- GastroPanel® should be used to rule out or confirm the high acid output of reflux patients instead of the trial and error use of PPIs. The long term use of PPIs may increase the risk of stomach and oesophageal cancer.
- GastroPanel® markers Pepsinogen I, PGI, Pepsinogen II, PGII, Gastrin-17, G-17 and *H.pylori* antibodies reveal:
    - Subjects at increased risk for stomach- and oesophageal cancer, i.e. those with atrophic gastritis as well as those with a low risk of cancer; *H.pylori* infection with no atrophic gastritis in the antrum or corpus.
    - Early and reliable diagnosis of *H.pylori* infection and atrophic gastritis (AG) save costs and prevent many unnecessary diseases and deaths due to stomach and oesophageal cancer.
- GastroPanel® is also indicated for special target patients, especially patients with autoimmune diseases (usually more than one at the same time), including, e.g.:
    - patients with autoimmune thyroiditis who may have autoimmune atrophic gastritis (AAG, 18% of thyroiditis patients) in the corpus with related risks,
    - patients with type 1 diabetes who may have AAG and, e.g., also deficiency of B-12 vitamin (12% of diabetes patients) with related risks,
    - patients with celiac disease who may have AAG with related risks, and
    - patients with rheumatoid arthritis who may have AAG with related risks.
- In patients with AG or AAG, absorption of vitamin B12 is reduced.
    - Due to vitamin B12 deficiency, there is an increased risk of depression, Alzheimer's disease, dementia and polyneuropathy. Consequently, all patients with depression, Alzheimer's disease, dementia and polyneuropathy should be examined by GastroPanel® to rule out or confirm those with AG or AAG in the corpus.
    - Due to vitamin B12 deficiency, increased homocysteine levels in the body may be related to:
        - Atherosclerosis – these patients should be examined by GastroPanel® to rule out or confirm AG or AAG with related risks
        - Heart attacks – these patients should be examined by GastroPanel® to rule out or confirm AG or AAG with related risks
        - Strokes – these patients should be examined by Gastro Panel® to rule out or confirm AG or AAG with related risks.
- Furthermore, in patients with AG or AAG of the corpus, absorption of Ca, Fe, Mg and Zn is reduced. Low Ca is associated with osteoporosis, while low serum Fe results in anemia.
- All osteoporosis and anemia patients should be examined by GastroPanel® to rule out or confirm AG or AAG.
- The risk of pneumonia and in senior citizens also the risk of fatal intestinal infections (such as giardiasis, malaria, *Clostridium difficile* and *E. coli* EHEC) may increase significantly due to an

anacidic stomach caused by AG, AAG or PPI's. All patients with such infections should be examined by GastroPanel® for detection of AG and AAG.

- All subjects diagnosed with AG and AAG in GastroPanel® need gastroscopy in order to confirm diagnosis and treatment.

Please note that the urea breath test (UBT), stool antigen test or *H.pylori* antibody test alone do not reveal AG or AAG. Furthermore, UBT and stool antigen test give 50% of false negative results in *H. pylori* patients, particularly if the patient has AG due to *H. pylori* infection or AAG, bleeding peptic ulcer, chronic use of PPIs, antibiotic treatment or MALT lymphoma due to *H. pylori* infection. GastroPanel® is also suitable for screening of healthy (asymptomatic) people, because *H. pylori* infection, AG or AAG with related risks are often asymptomatic.