Determination of *H. pylori*-related disease

A novel test panel enables a range of *H. pylori*-related diseases to be diagnosed.

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Australian doctors Barry J Marshall and J Robin Warren isolated *Helicobacter pylori* in 1982; this bacterium lives protected from gastric acids on the mucous membrane of the stomach. Infection with *H. pylori* usually occurs in childhood – rarely in adulthood; the infection spreads orally (oral-oral transmission) plus via the contents of the stomach (for example, by vomiting) and possibly also via the faeces. If untreated, the infection lasts for a lifetime and causes inflammation of the stomach, otherwise known as gastritis – in fact, virtually all cases of gastritis are caused by *H. pylori* infection. In a small number of cases, gastritis may develop as a result of an autoimmune disease. Over half of the global population suffers from infection with *H. pylori* and related gastritis (around 3,000 million people). In around half of the infected cases, the gastritis develops over the years into atrophic gastritis – that is, inflammation and atrophy of the mucous membrane of the stomach.

The isolation of *H. pylori* changed our understanding of the causes of gastric cancer and peptic ulcer. Today, it is known that *H. pylori* infection and gastritis are nearly always related to gastric cancer and peptic ulcer. Prior to 1982 – and even for a long time after that – it was believed that peptic ulcer developed primarily as a result of hypersecretion of acid, stress and anxiety.

In reality, in 70–90% of cases of peptic ulcer, the primary cause is gastritis or atrophic gastritis resulting from *H. pylori* infection. Other causes are anti-inflammatory analgesics (NSAID drugs) and aspirin. In 1994, a research unit operating under the WHO (the IARC – International Agency for Research on Cancer) presented a consensus statement, based on available research results, that gastric cancer was caused by *H. pylori* infection. Such infection was considered to be related to the development of gastric cancer (carcinogenicity class 1) in a similar way to the link between smoking and lung cancer. According to the consensus statement, *H. pylori* infection launches a chain of events, such as the development of atrophic gastritis, which in certain cases leads to gastric cancer.

Approximately 30% of the global population (nearly 2,000 million people) suffer from dyspepsia – that is, occasional or continuous pain or discomfort in the upper part of the stomach. The only method of determining whether a patient with dyspepsia or *H. pylori* infection is suffering from atrophic gastritis has, until now, been the histological (microscopic) examination of biopsies taken via gastroscopy. This invasive examination is often expensive, uncomfortable for the patient and limited in its availability; consequently, the patient is usually treated only on the basis of anamnesis,
symptoms or clinical examination. Many cases have demonstrated the unreliability of examinations made on the basis of symptoms – often leading to incorrect conclusions. Without a correct diagnosis, treatment may be delayed and the disease may even become impossible to cure; this may result in a decrease in the quality of life, and an increase in human suffering, healthcare costs and morbidity.

**H. pylori test panel**

Biohit has developed and patented a unique test panel (GastroPanel), which enables determination – from a blood sample – of whether a patient suffers from gastritis caused by *H. pylori*, whether the gastritis is atrophic and in which part of the stomach the changes are located. This is done by measuring the levels of Pepsinogen I and Gastrin-17, and *H. pylori* antibodies in the blood sample. The test panel enables identification of those patients whose risk of gastric cancer and peptic ulcer is considerably increased, and who need to be directed immediately to gastroscopy and examination of biopsy samples (1).

Research carried out to date has demonstrated that the results of the test panel are in practice as reliable as those obtained from gastroscopy and examination of biopsy samples. This applies to cases where it is necessary to find out whether the mucous membrane of the stomach is healthy, or whether it is inflamed or atrophic (atrophic gastritis). The research results support the argument that the test panel is suitable as an initial and easy method for examining dyspeptic patients. A correct diagnosis is nearly always reached – whether it is a case of a healthy, normally-functioning mucous membrane of the stomach, or whether it is inflamed, atrophic (atrophic gastritis) and not functioning normally.

Especially in cases of younger patients, over half of dyspeptic symptoms are functional (functional dyspepsia); these cases can be differentiated from organic symptoms by using the test panel. If the panel demonstrates that the mucous membrane is healthy, then this means that the symptoms are most likely to be functional and not caused by a peptic ulcer. The risk of gastric cancer and peptic ulcer is very low – nearly non-existent – if the stomach is healthy.

A multicentre study is currently being carried out in Finland in which gastroscopy and biopsy samples of a total of 204 patients suffering from dyspepsia have been examined. The results have demonstrated that the mucous membrane of 111 patients was normal, and only 20 patients suffered from advanced atrophic gastritis; when the blood samples of these patients were examined with Biohit’s test panel, the results were the same. The mucous membrane of the stomach of 73 patients was healthy or its surface was mildly inflamed (gastritis). On the basis of these examinations, it can be concluded that less than 10% of those examined (that is, 20 out of 204 patients) would have needed gastroscopy and examination of the biopsy samples immediately, due to gastritis and related risks and possible disease.
For interpretation of the results of the test panel, Biohit has developed an easy-to-use computer program, Biohit GastroSoft (2). On the basis of the laboratory results, the program draws up a recommended diagnosis of possible \textit{H. pylori} infection and atrophic gastritis. Moreover, the program indicates a patient’s risk of gastric cancer and peptic ulcer compared with the normal population; it further gives a recommendation based on the Maastricht 2000-consensus as to whether eradication therapy for \textit{H. pylori} is necessary, as well as an instruction as to whether gastroscopy, examination of biopsy samples and the measurement of vitamin B12 and homocysteine levels are necessary. (Atrophic gastritis can result in the malabsorption of vitamin B12 causing an increase in homocysteine levels. A deficiency in vitamin B12 is linked with conditions such as dementia, depression and damage to the peripheral nervous system, while an increased level of homocysteine is associated with a greater risk of arteriosclerosis, heart attacks and strokes.)

\textbf{Diagnosis, treatment and prevention of disease}

Biohit’s GastroPanel and related GastroSoft computer program are well suited for use by general practitioners and specialists in diagnosing \textit{H. pylori} infection and atrophic gastritis, as well as screening for the risk of gastric cancer and peptic ulcer from blood samples. The test panel also allows determination of whether conditions such as dementia, depression, heart attacks or stroke in a patient are linked to atrophic gastritis of the mucous membrane of the stomach. The rapid and early diagnosis of this connection is most important, as contributory or primary causes of such disease can be eliminated by therapy to eradicate \textit{H. pylori} infection. When levels of vitamin B12 and homocysteine are also determined as part of the test panel, it is possible to assess the risks related to diseases of the nervous and vascular systems.

In addition, the test panel provides an economic and easy means to differentiate between cases of functional dyspepsia and more severe diseases caused by atrophic gastritis. With over half of the world population infected by \textit{H. pylori}, and half of these cases leading to atrophic gastritis, a case could be made to justify routine use of the test panel in a similar manner to measuring blood pressure or cholesterol, or analysing blood count.

At present, \textit{H. pylori} infection is diagnosed worldwide using serological tests, breath tests and antigen tests of the faeces; these tests only enable diagnosis of whether a patient is infected or not. Biohit’s test panel represents a significant advance on these tests, as it enables the diagnosis of gastritis, its severity and quality almost as well as with gastroscopy and examination of biopsy samples. Tests conducted with the panel also facilitate assessment of the condition and functioning of the entire mucous membrane of the stomach – something which is not possible through histological examination of biopsy samples.

\textbf{Laboratory service}

In August 2001, Biohit started to offer a laboratory service (first in Finland and later in Biohit subsidiaries elsewhere) whereby blood samples are collected from medical centres and hospitals, and are then tested for Pepsinogen I and II, and \textit{Gastrin-17} concentrations, and \textit{H. pylori} antibodies using the test panel. Concentrations of vitamin B12 and homocysteine are also determined, as well as telomere DNA antibodies for the diagnosis of systemic lupus erythematosus (SLE). Furthermore, biopsies taken in connection with gastroscopy are used to diagnose lactose intolerance and to carry out further examinations, for example to confirm the diagnosis of gastric cancer and peptic ulcer. The laboratory will also engage in the research and development of diagnostic tests, and the analysis of different types of patient data.

Details of the tests performed by the laboratory and information about how to take and deliver samples can be obtained from Biohit plc: Email marianne.niemela@biohit.com, Fax +358-9-77386200, Tel +358-9-773861/Marianne Niemelä.

\textbf{References}

2. The program can be tested at www.biohit.com.