Serological assessment of samples from patients complaining of dyspepsia

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Many people consult their GP for upper gastrointestinal (GI) symptoms often associated with pain or burning and discomfort in the abdomen, and range from heartburn and acid regurgitation to nausea and vomiting.[1–3] These symptoms can cause problems with a person's physical and social activities and are generally related to the consumption of food and drink. Historically, these symptoms have been grouped together under the single term 'dyspepsia', meaning poor digestion.[4,5] Dyspepsia is defined as having one or more symptoms of epigastric pain, burning, post-prandial fullness or early satiation.[6]

One common cause of serious stomach problems is infection with *Helicobacter pylori*, which can be acquired at a young age and, without treatment, can colonise the stomach mucosa permanently.[7,8] In nearly half of *H. pylori*-infected cases, gastritis develops into atrophic gastritis (i.e., loss of glands and function of the stomach mucosa), which is most common in people aged over 50 years.

H. pylori infection and atrophic gastritis often cause no symptoms. Atrophic gastritis (AG) may be present in the upper stomach (corpus), in the lower stomach (antrum), or in both (Fig. 1). Atrophic gastritis of the corpus is linked with an increased risk of gastric cancer and of deficiencies in vitamin B_{12}, iron and calcium, all of which are associated with low acidity (hypochlorhydria) caused by atrophic gastritis.

In the antrum, atrophic gastritis is connected with an increased risk of gastric cancer and peptic ulcer disease. The risk of gastric cancer increases up to 90-fold if severe or moderate atrophy exists in both the antrum and corpus.[9–11] Normally, if patients have had a long history of symptoms they might require empirical treatment, endoscopy, testing for *H. pylori*, or a combination of these approaches.[12–14]

Quest Diagnostics has been offering the GastroPanel assays from BioHit (Laippatie 1, 08800, Helsinki, Finland) for patients referred to the walk-in clinic at the Upper Wimpole Street Laboratory complaining of dyspepsia. The GastroPanel is a panel of assays (pepsinogen I, gastrin 17 and *H. pylori*) and the results provide an algorithm which indicates stomach health and the function of the gastric mucosa.

Since commencing the service, the Quest Diagnostics' laboratory at Heston has examined 181 patients (age range: 19–75 years, median: 41 years). Of these, 105 (60.7%) were Japanese, 53 (30.6%) were European, and the remaining 15 (8.7%) an assortment of ethnicities. Of particular note among the Japanese group was the receipt of samples from 23 couples (husband and wife).

All of the assays were run in accordance with the kit instructions using appropriate external controls, which had been selected during the primary validation. The results were analysed using the Gastrosoft computer model and the reports produced were based on clinical studies comparing the results of GastroPanel examinations with results from gastroscopy and biopsy examination.

Of the 181 samples tested, 115 (68.4%) showed no abnormalities in the samples and were reported as 'normal function of gastric mucosa'. Thirty-six samples (20.7%) were positive for *H. pylori* alone and a report was issued with a recommendation to return to their GP and start an appropriate course of antibiotics. The remaining 30 samples showed a range of abnormal results (Table 1) and reports were issued with appropriate comment and recommendation to seek further advice.

Only 27 (14.9%) patients were over 50 years of age, 18 of which were reported as normal, four were positive for *H. pylori* alone, four showed increased pepsinogen I levels and the final sample – from a 51-year-old Japanese woman – was positive for both *H. pylori* and pepsinogen I.

When the GastroPanel examination gives a normal result for a healthy stomach mucosa, those patients suffering stomach problems usually have 'functional dyspepsia' or a disease process outside the stomach (e.g., in the colon) and can be directed to other types of testing and treatment.

About half of the world's population carries *H. pylori* and approximately half of these people will develop atrophic gastritis during their lifetime.[15] In atrophic gastritis, the cells and glands of the gastric mucosa are destroyed, causing serious structural and functional damage, and increasing the risk of many stomach-related diseases. Atrophic gastritis, a condition that is most commonly asymptomatic, can progress to gastric cancer. Although the incidence of gastric cancer is on the decline, it is still relatively common in the older age group as average lifespan increases.

Another important problem resulting from atrophic gastritis is deficiencies in vitamin B_{12}, iron, calcium and magnesium. It has been found that nearly half of those suffering from asymptomatic atrophic gastritis have vitamin B_{12} deficiency at the time of diagnosis, and possibly all atrophic gastritis patients will develop deficiency in time as vitamin B_{12} stores are depleted. Untreated vitamin B_{12} deficiency may cause permanent damage to the nervous system, resulting in depression and dementia. It may also cause an increase in homocysteine level, which is an independent risk factor for atherosclerosis and stroke. Iron

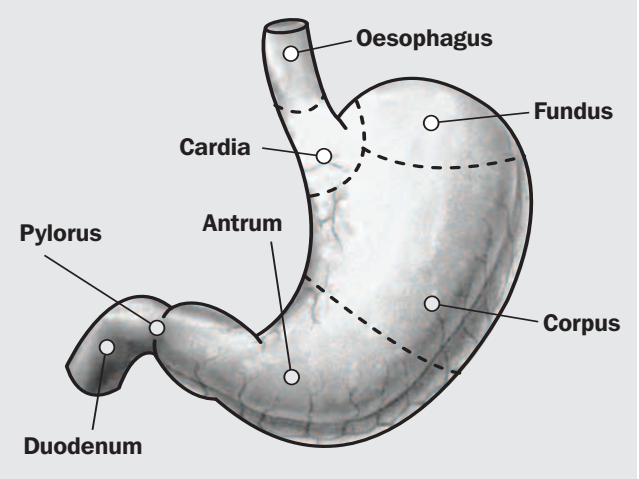

Fig. 1. Anatomy of stomach.

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Table 1. Abnormal sample results.

	Biomarker result			Report comment
Samples	Pepsinogen	G17	*H.pylori*	
4	Low (<30 μg/L)	Normal	Negative	Pepsinogen levels in the blood reflect the structure and function of the gastric corpus mucosa. When the mucosa undergoes atrophy, the level of pepsinogen falls below 30 μg/L.
8	High	High	Positive	Non-atrophic risk of gastritis, related to *H. pylori* infection. Increased risk of peptic ulcer disease (duodenal or gastric). •Treatment of *H .pylori* infection is recommended if successful therapy has not been given to the patient earlier. •High PGI value may indicate high acid output and/or ongoing PPI medication.
13	High	Normal	Negative	Pepsinogen levels in the blood reflect the structure and function of the gastric corpus mucosa. A high PGI may indicate high acid output or ongoing PPI medication.
5	High	High	Negative	Pepsinogen levels in the blood reflect the structure and function of the gastric corpus mucosa. A high PGI may indicate high acid output or ongoing PPI medication. Gastrin-17 level in the blood reflects the structure and function of the mucosa in the gastric antrum. The level of G17 in blood (fasting sample) falls when the acidity of the stomach increases (pH<2.5). A fasting G17 level below 1 pmol/L means that acid secretion is very high. A fasting level of G17 remains low also if there is atrophy of the antral mucosa, along with loss of antral G cells. If the fasting level of G17 is >10 pmol/L, it usually means the stomach is hypoacidic (i.e., low acidity due to PPI medication, or atrophy limited to corpus mucosa alone).

deficiency can cause anaemia, while calcium deficiency can result in osteoporosis. In addition to those suffering gastritis, patients with coeliac disease or the elderly on a poor diet may also suffer from these deficiencies.

The ability to differentiate between patients who have a healthy gastric mucosa and those showing signs of disease is useful in the diagnosis of atrophic gastritis. Gastroscopy and microscopy of endoscopic biopsies taken from the gastric antrum and corpus is a common approach to diagnosis; however, more recently, there have been advances in the use of a less-invasive option, the examination of gastric markers in serum or plasma.[16–19] The GastroPanel assay can be used to diagnose *H. pylori* infection and atrophic gastritis, and to estimate the risks associated with these conditions. Approximately half of the gastroscopies performed show healthy gastric mucosa and therefore the GastroPanel assay could save the patient from unnecessary discomfort and also reduce unnecessary healthcare costs. □

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