2. Lifestyle-Related Diseases and *Helicobacter pylori* Infection

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Following its establishment during childhood, *Helicobacter pylori* causes chronic inflammatory changes in the gastric mucosa, which leads to gastric ulcers, cancer, and mucosa-associated lymphoid tissue lymphoma (MALToma) in the stomach. In addition to various gastric diseases, *H. pylori* infection is reported to be related to various extra-gastric diseases, such as idiopathic thrombocytopenic purpura (ITP) and dermatitis. Further, the infection rate has been shown to be higher in patients with lifestyle-related ischemic heart and cerebrovascular diseases than in controls, and was suggested to be related to their development. Since those lifestyle-related diseases are caused by arteriosclerosis, there is significant interest in the relationship between arteriosclerosis and *H. pylori* infection.

In a previous study, we recruited over 1500 non-hospitalized subjects who received annual health checks, at which time we tested for the presence of *H. pylori* infection. When blood laboratory test results were compared between positive and negative subjects, the number of leukocytes was higher and HDL-cholesterol was lower in infected subjects, whereas serum total cholesterol, triglyceride, and homocysteine concentrations were not different (1, 2).

Another study of *H. pylori* infected subjects reported in the Western literature also found an increase in total cholesterol concentration. As a result, we repeated our study, using 900 subjects from a different city who were receiving an annual medical health check, and the results confirmed those of the previous study, as we found statistically significant differences only in the number of peripheral blood leukocytes and HDL-cholesterol concentrations (3).

A decreased concentration of HDL-cholesterol has been shown to be related to the development of arteriosclerosis, whose grade can be assessed by various non-invasive methods. One of the widely used methods is detection of atherosclerotic vascular walls with an ultrasonographic examination. This direct measurement of the changes in the arterial wall is accurate, however, a well-trained hand is required for accurate and reproducible results. Other methods include

ankle-brachial index (ABI) and pulse wave velocity (PWV). ABI is the ratio of blood pressure measured at the ankle compared to that at the brachial artery. If atherosclerotic stenosis is present in the large arteries between the ankle and brachial arteries, then the ratio will be decreased. Therefore, this method is useful for investigating atherosclerotic changes mainly in the large arteries and aorta. For determining ABI, the only procedure necessary is simultaneous measurement of blood pressure at two different sites and no special skill is required. PWV is the speed of pulse wave conductance between two arterial sites. When the arterial wall loses its elasticity and becomes stiff because of arteriosclerosis, the speed will increase. For determination, simultaneous measurement of pulse waves at two different arteries is necessary. Since ABI and PWV are relatively simple methods, it is possible to determine them by use of an automatic instrument. When we measured ABI, we found no difference between *H. pylori* infected and uninfected subjects. Therefore, *H. pylori* infection may not be related to the development of atherosclerotic stenosis of the arterial walls.

When we graded arteriosclerosis by measuring PWV, subjects with *H. pylori* infection had a higher conductance, suggesting a higher grade of arteriosclerosis (3), which demonstrated that subjects with *H. pylori* infection are prone to develop arteriosclerosis, and may have higher risk of cerebrovascular and ischemic heart diseases.

Gastroesophageal reflux disease (GERD) is caused by the pathological reflux of acidic gastric contents into the esophagus. In addition to causing obesity, high calorie meals and a fatty diet can induce such reflux. Therefore, GERD is considered to be a lifestyle-related disease and its prevalence is steadily increasing. *H. pylori* infection causes chronic inflammation in the stomach and a decrease in gastric acid secretion by destroying acid secreting parietal cells, thus it is protective against the occurrence of GERD.

The *H. pylori* infection rate is steadily decreasing in Japan, which is likely due to improvements in hygiene. According to an epidemiological study performed in the Shin-

shu area, the infection rate was remarkably decreased, especially in non-elderly subjects. This decreasing trend will lead to a decrease in number of cases with *H. pylori*-induced gastric mucosal inflammation and increase those with higher gastric acid secretion. In addition to the changes in the *H. pylori* infection rate, cases with higher gastric acid secretion are increasing, probably because of overall dietary changes (4). Because of the increased number of cases with higher gastric acid secretion along with fatty food-induced gastro-esophageal reflux, the number of cases with GERD is increasing rapidly in Japan.

Patients with GERD easily develop GERD-related complications, the most serious of which is Barrett's esophagus, a goblet cell intestinal metaplasia of the lower esophagus. As noted above, Japanese patients with GERD were found to have a significantly lower rate of *H. pylori* infection than controls. Further, the infection rate in patients with Barrett's esophagus has been shown to be much lower than in controls in studies performed in Western countries. Therefore, the decreased rate of *H. pylori* infection may have a significant impact on the recent increase in Barrett's esophagus

cases, who progress to esophageal adenocarcinoma at a rate of 0.5% each year. Therefore, subjects without *H. pylori* infection are prone to develop esophageal adenocarcinoma via GERD and Barrett's esophagus. Although the number of cases with esophageal adenocarcinoma is still quite low in Japan, it may increase in the near future, as the number of cases with GERD began to show an increase approximately 20 years ago. Therefore, close attention must be given to any increase in the number of esophageal adenocarcinoma cases.

To summarize, *H. pylori* infection may be related to the development of two different lifestyle-related diseases. Infected subjects can easily develop arteriosclerosis, resulting in cerebrovascular and ischemic heart diseases, while the absence of infection can also lead to the development of GERD and the resulting esophageal adenocarcinoma. An epidemiological study done in UK showed that patients with Barrett's esophagus tended to have a lower risk for developing stroke. Additional research is necessary to further elucidate the relationship between *H. pylori* infection and lifestyle-related diseases.

References

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