Association of *Helicobacter pylori* with gastric carcinoma

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Helicobacter pylori is a nonsporing curvilinear gram negative rod of size approximately 3.5 × 0.5µm and found to be associated with the development of chronic antral gastritis, gastroduodenal ulcers, gastric cancer and mucosa- associated lymphoid tumors. In 1983, ***Marshall*** and ***Warren*** discovered this unidentified curved bacillus located on the gastric epithelium of patients with chronic active gastritis. The discovery of Helicobacter pylori and its association with a number of gastrointestinal diseases has revolutionized the field of gastroenterology.

It is well established that cancer arises in chronically inflamed tissue, and this is particularly notable in the gastrointestinal tract. Classic examples include Helicobacter pylori-associated gastric cancer and inflammatory bowel disease-associated colorectal cancer. Helicobacter pylori infection is basically acquired during infancy and persists for decades together. The mode of transmission has not been well defined, although oral-oral transmission, fecal oral transmission and environmental spread are among the possible routes. Bacteria, which are closely associated with gastric epithelial cells and in the mucous layer, are mainly present in the antrum but also found in the patches of gastric metaplasia in the duodenum and the esophagus.

H pylori infection is proposed to be involved in the development of gastric cancer. The high prevalence of *H pylori* infection in early age groups increases the risk of gastric cancer. Many studies showed a significant correlation of gastric cancer with the raised concentration of IgG antibodies to *H pylori*. Clinical studies based on histo-pathological examination of gastric biopsy specimens showed that *H pylori* infection is more common in patients with gastric cancers than patients with no pathological lesions. Severe atrophy of the stomach and the foci of gastric metaplasia, which precede the development of gastric tumors result in reduced colonization of *H pylori.* In these circumstances a biopsy specimen may be negative while, for several years IgG antibodies would remain positive indicating evidence of past infection.

Despite a possible role of *Helicobacter pylori* in gastric carcinoma (GC), its pathogenesis is not clear. Integrity of tissues, including that of gastric epithelium, is maintained by a balance between cell death by apoptosis or necrosis and regeneration. This balance may be altered by *H. pylori* infection, since it induces apoptosis of gastric epithelial cells both *in vivo* and *in vitro*. The studies from the developed world suggest that CagA-bearing strains of *H. pylori* are more often associated with gastroduodenal diseases than CagA-negative strains. It is becoming clearer that H. pylori strains carrying a functional Cag pathogenicity island (cagPAI), which encodes the type IV secretion system (TFSS) and its effector CagA, play an important role in the development of gastric carcinoma. Pathomechanism of gastric carcinogenesis associated with H. pylori includes bacteria-host interaction leading to morphologic alterations such as atrophic gastritis and gastrointestinal metaplasia mediated by COX-2 overexpression, cancer cell invasion, and neo-angiogenesis via TLR2/TLR9 system and transcription factors (e.g., NF-kappaB) activation.

Long standing mucosal inflammation reduces acid secretion (hypochlorhydria) and pepsin secretion. This favors bacterial growth and sustained mucosal epithelial cells proliferation, which increases risk of genomic mutation. DNA damage is further contributed by increased oxidative stress. How a person becomes infected with *H pylori* is not yet fully understood. The factors that affect the risk of a subject acquiring such infection and methods of prophylaxis have also not been identified with any certainty. Further studies are required in this field that would be helpful to prevent gastric cancers. The eradication of this pathogen, in children as well as in adults, should theoretically lead to the disappearance of gastric cancer.

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