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Helicobacter Pylori-An emerging silent killer

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INTRODUCTION

Helicobacter-related gastric diseases occur in humans from an explosion in research, which occurred after the first culture by Marshall and Warren in 1982**[1].**The presence of spiral-shaped micro-organisms in stomach mucosa was described almost 100 years ago**[2].**This discovery rapidly revolutionized the discipline of gastroenterology in human medicine and identified it as the causative agent of gastritis and peptic ulcer **[3].**

Helicobacter pylori is now regarded as the most widespread infection in man: it has a world-wide distribution and it is estimated that approximately two-thirds of the entire world's population is infected with this pathogen **[4]**. Most infections are believed to be acquired during childhood and appear to persist for decades **[5]**. H. pylori are known to be the most important causal agent of human gastritis, gastric and duodenal ulcers, and have recently been classified as a first class human carcinogen by IARC (International Agency for Research on Cancer) (Anonymous, 1994).
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The primary disorder, which occurs after colonization with H. pylori, is chronic active gastritis. This condition can be observed in all H. pylori -positive subjects. The intragastric distribution and severity of this chronic inflammatory process depend on a variety of factors, such as characteristics of the colonizing strain, host genetics and immune response, diet, and the level of acid production. H. pylori -induced ulcer disease, gastric cancer, and lymphoma are all complications of this chronic inflammation, ulcer disease and gastric cancer in particular occur in those individuals and at those sites with the most severe inflammation. Understanding of these factors is thus crucial for the recognition of the role of H. pylori in the etiology of upper gastrointestinal pathology.

The gastric mucosa is well protected against bacterial infections. H. pylori is highly adapted to this ecologic niche, with a unique array of features that permit entry into the mucus, swimming and spatial orientation in the mucus, attachment to epithelial cells, evasion of the immune response, and, as a result, persistent colonization and transmission. To colonize the stomach, H. pylori must survive the acidic pH of the lumen and use its flagella to burrow into the mucus to reach its niche, close to the stomach's epithelial cell layer**[6].** Many bacteria can be found deep in the mucus, which is continuously secreted by mucus-secreting cells and removed on the luminal side. To avoid being carried into the lumen, H. pylori sense the pH gradient within the mucus layer by chemotaxis and swims away from the acidic contents of the lumen towards the more neutral pH environment of the epithelial cell surface **[7].**

To survive in the presence of acid produced in the stomach H. pylori has to counteract this acidic environment. H. pylori produce an important enzyme, urease, which hydrolyses urea into NH 3 and CO 2. This enzyme has an essential role in the H. pylori infection as observed in urease-defective bacteria mutants which cannot colonize the stomach **[8]**. Urease causes damage to the epithelium through the production of ammonia, that in conjunction with neutrophil metabolites , form carcinogenic agents that might participate in the development of gastric malignances **[9].** Ammonia is capable of causing different cell alterations, including swelling of intracellular acidic compartments, alterations of vesicular membrane transport, repression of protein synthesis and ATP production, and cell-cycle arrest **[10]**. Urease might also help to the recruitment of neutrophils and monocytes in the mucosa and to the production of pro-inflammatory cytokines **[11]**.

Clinical features :
Chronic H. pylori –associated gastritis per se is asymptomatic but the initial acquisition of the infection cause acute gastritis with hypochlorhydria which may cause abdominal pain, nausea and vomiting that resolve within a few days **[12]**. Uncomplicated peptic ulcers typically cause epigastric pain and less commonly, nausea, vomiting and weight loss, whereas some ulcers (particularly NSAID ulcers) are asymptomatic. The classically described pain of duodenal ulcer is felt as a growing or burning sensation, often with a relation to meals; occurring 1-3 hours after meals and /or at night and relieved by food. Gastric ulcer pain is instead often precipitated by food. However symptoms are actually very poorly discriminatory for ulceration site and even for whether or not an ulcer is present. Examination usually reveals epigastric tenderness but may be normal.

H. pylori related pathological conditions:
Although gastric colonization with H. pylori induces histologic gastritis in all infected individuals, only a minority develop any apparent clinical signs of this colonization. It is estimated that H. pylori -positive patients have a 10 to 20% lifetime risk of developing ulcer disease and a 1 to 2% risk of developing distal gastric cancer **[13]**. The risk of development of these disorders in the presence of H. pylori infection depends on a variety of bacterial, host, and environmental factors that mostly relate to the pattern and severity of gastritis.

Acute and chronic gastritis : Many studies convincingly demonstrate that H.pylori colonization of the gastric mucoza is associated with gastritis, with chronic inflammatory cell infiltrate. The macroscopic nodular gastritis was significantly associated with active chronic gastritis and follicular gastritis. Colonization of the gastric antrum by H.pylori is graded as mild, moderate or marked **[14]**. Chronic H. pylori –associated gastritis per se is asymptomatic but the initial acquisition of infection cause acute gastritis with hypochlorhydria which may cause abdominal pain, nausea and vomiting that resolve within a few days **[15].**

Peptic ulcer disease (PUD) :Gastric or duodenal ulcers (commonly referred to as peptic ulcers) are defined as mucosal defects with a diameter of at least 0.5 cm penetrating through the muscularis mucosa. Gastric ulcers mostly occur along the lesser curvature of the stomach, in particular, at the transition from corpus to antrum mucosa **[16]**. Both gastric and duodenal ulcer diseases are strongly related to H. pylori infection. In initial reports from all over the world in the first decade after the discovery of H. pylori , approximately 95% of duodenal ulcers and 85% of gastric ulcers occurred in the presence of H. pylori infection **[17]**.Several cohort studies estimated that the lifetime risk for ulcer disease sin H. pylori -positive subjects is 3 to 10 times higher than in H. pylori -negative subjects **[18]** and that 10 to 15% of H. pylori -positive subjects developed ulcer disease during long-term follow-up .Eradication of H. pylori dramatically changes the natural course of ulcer disease and almost completely prevents ulcer recurrence **[19].**

Non-ulcer dyspepsia: Non-ulcer or functional dyspepsia is defined as the presence of symptoms of upper gastrointestinal distress without any identifiable structural abnormality during diagnostic work-up, in particular including upper gastrointestinal endoscopy. Thirty (30%) to 60% of patients with functional dyspepsia carry H. pylori, but this prevalence is not much different from that in the unaffected population **[20].**

Atrophic gastritis, intestinal metaplasia, and gastric cancer: Chronic H. pylori -induced inflammation can eventually lead to loss of the normal gastric mucosal architecture, with destruction of gastric glands and replacement by fibrosis and intestinal-type epithelium. This process of atrophic gastritis and intestinal metaplasia occurs in approximately half of the H. pylori -colonized population, first in those subjects and at those sites where inflammation is most severe **[21]**. The risk for atrophic gastritis depends on the distribution and pattern of chronic active inflammation. As such, subjects with decreased acid output show a more rapid progression towards atrophy**[22]**. Areas of gland loss and intestinal metaplasia extend with time multifocally, and although they do not give rise to any specific symptoms, they increase the risk for gastric cancer by 5- to 90-fold depending on the extent and severity of atrophy **[23].**

Evidence that H. pylori increases the risk of gastric cancer development via the sequence of atrophy and metaplasia originates from various studies, in which it was shown that H. pylori-positive subjects develop these conditions more often than do uninfected controls **[24].** This is supported by data that showed geographical associations between the prevalence of H. pylori and the incidence of gastric cancer **[25]** The Eurogast Study Group, 1993. The risk of development of atrophy and cancer in the presence of H. pylori is again related to host and bacterial factors, which influence the severity of the chronic inflammatory response. As such, the risk is increased in subjects colonized with cagA -positive strains **[26][27]**, but also in those with a genetic predisposition to higher IL-1 production in response to colonization **[28]**.

Gastric MALT lymphoma: The association of H. pylori and MALToma is an established fact. The gastric mucosa does not normally contain lymphoid tissue, but MALT nearly always appears in response to colonization with H. pylori. In rare cases, a monoclonal population of B cells may arise from this tissue and slowly proliferate to form a MALT lymphoma. Nearly all MALT lymphoma patients are H. pylori positive **[29]**, and H. pylori -positive subjects have a significantly increased risk for the development of gastric MALT lymphoma **[30]**. Because of the diagnostic controversies and the relative rarity of this disorder, the exact incidence in H. pylori -positive subjects is unknown, but MALT lymphomas occur in less than 1% of H. pylori -positive subjects**[31].**

Gastro-esophageal reflux disease (GERD): Yet another highly controversial topic is the role of H. pylori in the pathogenesis of gastro-esophageal reflux disease (GERD). Some studies suggest that H. pylori protects human subjects from developing GERD **[32]**, whereas others postulate a causative association between them. Some studies have identified an association between the CagA-positive strains and the increased acid secretion that in turn leads to gastro-esophageal reflux **[33]**. The causative association between H. pylori and GERD needs further research for confirmation.

Extragastroduodenal disorders: H. pylori has been linked to a variety of extragastric disorders. These include coronary heart disease, dermatological disorders such as rosacea and idiopathic urticaria, autoimmune thyroid disease and thrombocytopenic purpura, iron deficiency anemia, Raynaud phenomenon, scleroderma, migraine, and Guillain-Barré syndrome. The underlying hypothetical mechanisms include chronic low-grade activation of the coagulation cascade, accelerating atherosclerosis, and antigenic mimicry between H. pylori and host epitopes leading to autoimmune disorders **[34].**

Growth faltering in children: Several studies have shown that H. pylori infection in childhood is associated with growth faltering **[35][36]**. However, these studies are confounded by the coexistence of variables such as poor socioeconomic status, which may contribute to both the development of malnutrition and the early H. pylori colonization. Therefore, H. pylori and growth faltering may be mere associations rather than cause and effect.

Infection with H. pylori causes chronic inflammation and significantly increases the risk of developing duodenal and gastric ulcer disease and gastric cancer. Infection with H. pylori is the strongest known risk factor for gastric cancer, which is the second leading cause of cancer-related deaths worldwide.

REFERENCES

[1] Warren JR and Marshall B. Unidentified curved bacilli on gastric epithelium in active chronic gastritis. Lancet . 1983; 321 : 1273-1275.
[2] Madan E, Kemp J, WestblomU . Evaluation of staining methods for identifying Campylobacter pylori. American J Clin Pathol . 1988; 90 : 450-453.
[3] Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and ulceration. Lancet 1984; i: 1311-1315.
[4] Dunn BE, Campbell GP, Perez-Perez GI . Purification and characterization of urease from Helicobacter pylori . J Biol Chem . 1990; 265 : 9464-9469.
[5] Blaser MJ and JE. Crabtree. CagA and the outcome of Helicobacter pylori infection. American J Clin Pathol .1996; 106 : 565-567.
[6] Amieva MR, El-Omar EM. Host-bacterial interactions in Helicobacter pylori infection. Gastroenterology. 2008; 134 (1):306–23.
[7] Schreiber S, Konradt M, Groll C . The spatial orientation of Helicobacter pylori in the gastric mucus. Proc Natl Acad Sci. U.S.A. 2004; 101 (14): 5024–9.
[8] Montecucco C &Rappuoli R. Living dangerously: how Helicobacter pylori survives in the human stomach. Nat Rev Mol Cell Biol. 2001; 2: 457-466.
[9] Suzuki M, Miura S, Suematsu M. Helicobacter pylori-associated ammonia production enhances neutrophil-dependent gastric mucosal cell injury. Am J Physiol. 1992; 263 : G719-725.
[10] Montecucco C &Rappuoli R. Living dangerously: how Helicobacter pylori survives in the human stomach. Nat Rev Mol Cell Biol. 2001; 2: 457-466.
[11] Harris AW, Douds A, Meurisse EV . Seroprevalence of Helicobacter pylori in residents of a hospital for people with severe learning difficulties. Eur J Gastroenterol Hepatol. 1995; 7: 21-23.
[12] Fischer W, Puls J, Buhrdorf R. Systematic mutagenesis of the Helicobacter pylori cag pathogenicity island: essential genes for CagA translocation in host cells and induction of interleukin-8. Mol Microbio . 2001; l42 : 1337-1348.
[13] Kuipers EJ, Thijs JC and Festen HG. The prevalence of Helicobacter pylori in peptic ulcer disease. Aliment PharmacolTher . 1995; 9(2): 59-69.
[14] Uc A, Chong SK. Treatment of Helicobacter pylori gastritis improves dyspeptic symptoms in children. J Pediatr Gastroenterol Nutr . 2002; 34 : 281–5.
[15] Fischer W, Puls J, Buhrdorf R. Systematic mutagenesis of the Helicobacter pylori cag pathogenicity island: essential genes for CagA translocation in host cells and induction of interleukin-8. Mol Microbio . 2001; l42 : 1337-1348.
[16] Veldhuyzen van Zanten SOJ, Dixon MF and Lee A. The gastric transitional zones: neglected links between gastroduodenal pathology and Helicobacter ecology. Gastroenterology . 1999; 116 : 1217-1229.
[17] Kuipers EJ, Thijs JC and Festen HG. The prevalence of Helicobacter pylori in peptic ulcer disease. Aliment PharmacolTher . 1995; 9(2): 59-69.
[18] Nomura A, Stemmermann GN, Chyou PH . Helicobacter pylori infection and the risk for duodenal and gastric ulceration. Ann Intern Med. 1994; 120 : 977-981
[19] Hessay SJ, Spencer J, Wyatt JI . Bacterial adhesion and disease activity in Helicobacter associated chronic gastritis. Gut. 1990; 31: 134–138.
[20] Talley NJ and Hunt RH. What role does Helicobacter pylori play in dyspepsia and nonulcer dyspepsia? Arguments for and against H. pylori being associated with dyspeptic symptoms. Gastroenterology . 1997; 113 : 67-77.

[21] Kuipers EJ, Thijs JC and Festen HG. The prevalence of Helicobacter pylori in peptic ulcer disease. Aliment PharmacolTher . 1995; 9(2): 59-69.
[22] Kuipers EJ, Lundell L, Klinkenberg-Knol EC . Atrophic gastritis and Helicobacter pylori infection in patients with reflux esophagitis treated with omeprazole or fundoplication. N Eng J Med. 1996; 334 : 1018-1022.
[23] Sipponen P, Kekki M, Haapakoski J . Gastric cancer risk in chronic atrophic gastritis: statistical calculations of cross-sectional data. Int J Cancer. 1985; 35 : 173-177.
[24] Kuipers EJ. Review article: relationship between Helicobacter pylori , atrophic gastritis and gastric cancer. Aliment PharmacolTher . 1998; 12 : 25-36.
[25] Forman D, SitasF, Newell DG . Geographic association of Helicobacter pylori antibody prevalence and gastric cancer mortality in rural China. Int J Cancer. 1990; 46 : 608-611.
[26] Kuipers EJ, Thijs JC and Festen HG. The prevalence of Helicobacter pylori in peptic ulcer disease. Aliment PharmacolTher . 1995; 9(2): 59-69.
[27] Parsonnet J, Friedman GD, OrentreichN . Risk for gastric cancer in people with CagA positive or CagA negative Helicobacter pylori infection. Gut. 1997; 40 : 297-301.
[28] Amieva MR, El-Omar EM. Host-bacterial interactions in Helicobacter pylori infection. Gastroenterology. 2008; 134 (1):306–23.
[29] Eidt S, Stolte M and Fischer R. Helicobacter pylori gastritis and primary gastric non-Hodgkin's lymphomas. J Clin Pathol . 1994; 47 : 436-439.
[30] Parsonnet J, Hansen S, Rodriguez L . Helicobacter pylori infection and gastric lymphoma. N Engl J Med. 1994; 330 : 1267-1271.
[31] Parsonnet J, and Isaacson PG. Bacterial infection and MALT lymphoma. N Engl J Med . 2004; 350 : 213-215.
[32] Perez-Perez, GI, Dworkin BM, Chodoes JE and Blaser MJ. Campylobacter pylori antibodies in humans. 1988; Ann. Intern. Med. 109;11-17.
[33] Fallone CA, Barkun AN, Gottke MU . Association of Helicobacter pylori genotype with gastroesophageal reflux disease and other upper gastrointestinal diseases. American J Gastroenterol. 2000; 95 : 659-669.
[34] Gasbarrini A, Carloni E, GasbarriniG . Helicobacter pylori and extragastric diseases—other Helicobacters. Helicobacter. 2004; 9(1): 57-66.
[35] Goggin PM, Hawtin P, Fine D . Growth in infancy, infant feeding, childhood living conditions, and Helicobacter pylori infection at age 70. Arch Dis Child. 1997; 77: 310–4.
[36] Correa P, Fonthan EE, Reina JC. Effects of a new Helicobacter pylori infection on height and weight in Colombian children. Ann Epidemiol. 2006; 16 : 347–51.