

# *Helicobacter pylori* infection and gastric carcinogenesis

Peter Malfertheiner

*Otto-von-Guericke-University, Department of Gastroenterology, Hepatology and Infectious Diseases, Magdeburg, Germany*

The major and threatening complications from *Helicobacter pylori* infection is gastric cancer. The disease occurs usually at a more advanced age (> 50 years) and at the time of clinical presentation it is in most cases (~ 85%) a non curable condition. Frequently there are no premonition symptoms and therefore prevention strategies offer the best chance. *H. pylori* testing with treatment in case of a positive result in dyspeptic patients, although an important strategy, would not permit to prevent gastric cancer in a large number of patients as many are not dyspeptic before gastric cancer becomes apparent. Screen and treat would be the best strategic option but has currently the limits of therapy which is still complex and difficult to prescribe for asymptomatic persons with the scope of prevention. Moreover, these strategies would incur a huge burden of expenses currently not acceptable by health regulatory organs. The best imaginable approach for current application is test and treat complemented by a search and treat strategy in subsets of patients at risk.

According to epidemiological data approximately 70% of distal gastric cancers can be attributed to *H. pylori*. The evidence for *H. pylori* as the most important risk factor in gastric cancer is based on biological plausibility and on the beneficial effect of eradication on the progression from gastritis to gastric cancer. Experimental investigations in animal models and from numerous studies with human tissues and cells provide further support for the causal association of *H. pylori* with gastric cancer.

*H. pylori* infection interferes with cell biological phenomena that are linked with gastric carcinogenesis. It triggers hyperproliferative and apoptotic processes and takes direct command of the epithelial cell signalling including the modulation of tyrosine-kinase receptors, activation of cell dissociation as well as disruption of cell-cell interactions.

Only a subset of individuals will develop malignant *H. pylori*-related disease. At present, there are few predictors for an increased gastric cancer development

---

Prof. Peter Malfertheiner, M.D., *Director*  
Department of Gastroenterology, Hepatology and Infectious Diseases  
Leipziger Straße 44  
DE-39120 Magdeburg, Germany  
Phone: +49 391 67 13 100  
Contact e-mail: [daniela.deutschlaender@medizin.uni-magdeburg.de](mailto:daniela.deutschlaender@medizin.uni-magdeburg.de)

among the infected. Microbial and host factors, together with the environment, seem to determine which groups of individuals will develop gastric cancer. Certain *microbial* virulence factors such as the Cag PAI (Pathogenicity island), Vac alleles as well as other bacterial molecules are more prevalently found in bacteria isolated from patients with gastric cancer.

*Host genetic factors* are related to functional polymorphisms of various genes and also contribute significantly to the clinical outcome of *H. pylori* infection. These factors relate to the host immune and inflammatory response against the bacterium. There is an important interaction between host genetic factors and *H. pylori* virulence determinants. Functional polymorphisms in the interleukin-1 beta (IL-1B-511/-31), tumour necrosis factor alpha

(TNF-A-308) genes and others significantly increase the risk of non-cardia gastric cancer.

The risk appears to be significantly increased in the presence of certain genotypes of various pro-inflammatory cytokines and of *H. pylori* strains with higher virulence. Furthermore, the increased risk applies equally to intestinal and diffuse types of gastric adenocarcinoma.

Future tasks are: better definition of subjects at risk, identify the point of no return in the pathway of gastric carcinogenesis despite *H. pylori* eradication, and development of a novel therapy (the golden bullet).

A strategy scenario I could imagine is to screen all children at school age and treat all positive with a simple well tolerated new drug.