Healthcare industry BW

Manfred Kist – 25 years of fascination for a stomach bacterium

Helicobacter pylori is a genus of bacteria that inhabits the human stomach. The bacteria can cause duodenal and gastric ulcers and are also linked to the development of gastric cancer. Prof. Dr. Manfred Kist from the Freiburg University Medical Centre has spent around 25 years of his scientific career on investigating H. pylori, a bent, rod-shaped bacterium. Kist sees H. pylori primarily as an organism that is extremely well adapted to adverse living conditions and that has turned into a dangerous pathogen as a result of changes in human life. Prof. Kist, who is to retire next year, is fascinated by the bacterium's biology. Moreover, he wants to help patients suffering from H. pylori infections. The head of the National Centre for Helicobacter pylori advocates the differentiated treatment of infected patients because he is convinced that the microbes do not cause problems in all cases.

Gastric acid is able to destroy Helicobacter pylori. However, the bacteria have found strategies to prevent themselves from destruction: flagella and the helical shape enable the bacteria to move around in the stomach. If necessary, they intrude the gastric mucosa where a pH prevails that is better suited to their requirements. Helicobacter pylori requires the protective environment of the gastric epithelium to survive; it does not survive in the intestines due to the presence of bile acid. "However, the stomach is anything else but a quiet place," said Prof. Dr. Manfred Kist, deputy head of the Department of Medical Microbiology and Hygiene at the Freiburg University Medical Centre and head of the National Reference Centre for Helicobacter pylori. "The conditions in our stomach change dramatically whenever we eat something; the gastric acid level rises and the concentration of toxic metal ions such as nickel, iron and copper increases." It is assumed that humans became infected with H. pylori around 150,000 years ago and that the bacteria have been able to adapt to these inhospitable conditions since that time. At a low pH, H. pylori cleaves urea to produce energy and important nutrients as well as alkaline ammonium ions that lead to a pH increase in neighbouring areas.

A complex jack of all trades

Prof. Dr. med. Manfred Kist
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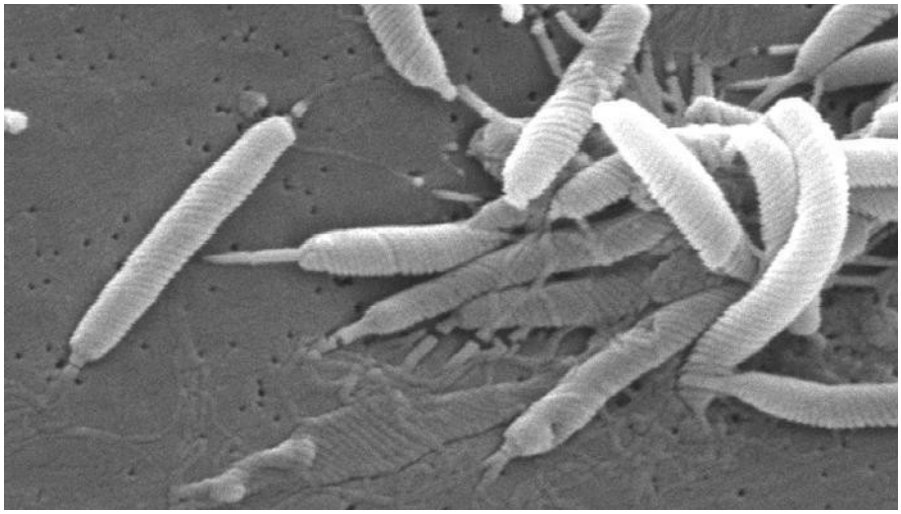
Kist has spent 25 years of research on investigating the bacteria's adaptation mechanisms, including on the molecular level. Kist, who was born in Bühl (Baden) in 1946 and studied medicine in Freiburg between 1966 and 1971 and received his PhD in microbiology in 1973, has for a long time been interested in the interaction of microbes and mucosae. Initially, he was focussed on mycoplasmas, but later on he turned to Helicobacter pylori, a genus of bacteria that was hardly known back then. Kist and his team at the Institute of Medical Microbiology and Hygiene in Freiburg gradually discovered molecular responses to elevated gastric iron and nickel levels. They found that complex signalling networks inside the organism activate molecules that form complexes with metal ions inside the cells or pump them out of the cell, thereby making them harmless. Kist also found that Helicobacter is not a pathogen per se, but that it developed into one under suitable conditions. It seems that, amongst other things, the increasing life expectancy of humans was a crucial factor in this development.

Although H. pylori has adapted quite well to life in the human stomach, the bacteria are not that fond of the gastric acid, as it may seem. In people producing large amounts of acid, H. pylori colonises the stomach antrum to avoid the hydrochloric-acid secreting parietal cells located in the main body (corpus) of the stomach. However, the inflammatory response to H. pylori induces specific cells in the antrum to produce a hormone that stimulates the parietal cells in the corpus to secrete even higher amounts of acid into the stomach. The increased acid load of the stomach makes H. pylori enter the intestines, thereby leading to damage of the duodenum (duodenal ulcer). This would remain the only problem if people did not live longer than 40 years. In contrast, H. pylori infections are also associated with stomach cancer, especially in people who produce too little acid, something that is typical for people over 40 in whom the parietal cells gradually cease to produce hydrochloric acid. In these people, H. pylori can colonise the stomach corpus where the acid-secreting parietal cells are located. Chronic inflammation, therefore, leads to the destruction of the parietal cells, the further reduction of acid production and the accumulation of H. pylori, and the shrinking and loss of the cells in the stomach, i.e. atrophy of the stomach lining, which might lead to gastric ulcer and increase the risk of gastric cancer cancer. Moreover, bacteria from the oral cavity and the intestines invade the stomach.

"Atrophy of the stomach is considered to be a precancerous condition," said Kist going on to add that "since this condition depends on the age of the people affected, a population with individuals that are younger than 40 is hardly ever affected by gastric cancer." Kist has developed a general model for human infections from the aforementioned findings: people do not get ill just because they are infected with bacteria. Infections occur only if many favourable factors coincide: the pathogens, the condition of the host and the environmental conditions. Improved medical treatment in industrialised countries has led to an increase in life expectancy, which has also led to an increase in the incidence of gastric cancer. In addition, people tend to eat more, which causes excess gastric acid production. Therefore, the risk of developing duodenal cancer below the age of forty has considerably increased in recent years.

Differentiated process to assess infections

Therefore, Helicobacter pylori must not per se be considered a pathogen. "In principle, we might even say that it was once part of people's natural gastric flora," said Kist alluding to the finding that H. pylori has adapted itself to the human immune system. Although the immune system recognises H. pylori as an intruder,



Electron microscope image of helical rod-shaped Helicobacter pylori bacteria.
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it recognises it far less efficiently than other microorganisms. It is known that typical Helicobacter surface structures (lipopolysaccharides) induce an around 100 times weaker immune reaction than those of Escherichia coli, which is commonly found in the human intestines. "Although we are able to react to an infection with H. pylori, we are unable to eliminate the bacteria completely. It seems as if the bacteria have found ways to not induce too strong an inflammatory reaction in humans."

Since H. pylori infections do not always lead to gastric cancer and because the treatment of duodenal ulcers is relatively successful, Kist supports the idea of looking at Helicobacter infections on a case-to-case basis. “Sixty per cent of individuals infected with Helicobacter pylori are asymptomatic, i.e. never show any signs of disease,” said Kist. Antibiotic treatment of H. pylori infections can have severe side effects, including the development of antibiotic resistance of other bacterial species, something that might become very dangerous. As the head of the National Reference Centre for Helicobacter pylori, which Kist established in 2000, Kist has supported the preparation new H. pylori treatment guidelines that stipulate diagnosis and treatment depending on the patients’ individual requirements. The guidelines recommend that doctors treat intestinal and gastric ulcers as soon as these diseases are diagnosed. If a patient produces too little acid and is, therefore, at greater risk of developing gastric cancer, treatment recommendations also need to be based on additional factors such as the incidence of such cancers in the patient’s family.

“There is no single therapy available that would be suitable to treat all the types of Helicobacter infections,” said Kist summarising his experiences. “Each case must be assessed on the basis of valid guidelines and the individual patients be treated accordingly.” Prof. Dr. med. Manfred Kist will retire in summer 2011, but will be able to look back on great achievements in that he has developed a comprehensive picture of his research object, which reflects the entire complexity of the reality, and that will lead to more effective strategies to treat Helicobacter infections.

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