

LETTER

***Helicobacter pylori* and Pancreatic Cancer. A Working Hypothesis from Epidemiological Studies**

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Dear Sir:

We have read the informative article about *Helicobacter pylori* (HP) and pancreatic disease written by Manes *et al.* with great interest [1]. We were, however, slightly puzzled by the statement that no data on a potential association between *Helicobacter pylori* infection and pancreatic cancer are available. According to recent data, two articles and one letter about an association between the bacteria and pancreatic cancer have been published. In the first study on this topic published in 1998, we compared the HP seroprevalence rate in 92 patients with pancreatic carcinoma and 92 matched control subjects [2]. In total, 65% of the pancreatic cancer patients were found to be seropositive, while only 45% of the control group without gastric cancer tested positive. These results were statistically significant (P=0.035) indicating an odds ratio of 2.1 (95% CI: 1.1-4.1) in the seropositive cohort and suggesting a positive association between HP infection and pancreatic adenocarcinoma. Microscopic evaluation of 20 resection specimens available from these patients, however, revealed no evidence of the presence of HP in pancreatic (cancer) tissue as judged by light microscopy.

In 2001, a case control study about the association of HP carriage and exocrine pancreatic cancer in 29,133 male Finnish smokers was published by Stolzenberg-

Solomon *et al.* [3]. In keeping with our initial data, HP positive individuals were at statistically significantly elevated risk of pancreatic cancer as compared to the negative cohort. In addition, an odds ratio of 1.87 (95% CI: 1.05-3.34) was found, which is similar to the risk attributed to HP infection in our much smaller study [2]. In addition, Nilsson *et al.* [4] have reported identification of the *Helicobacter* species in the livers of patients with hepatocellular and cholangiocellular carcinoma. According to the serologic data [2, 3], they have extended their analyses to normal and malignant pancreatic tissue. While attempts to cultivate *Helicobacter* species were unsuccessful, PCR for *Helicobacter* was positive in 5 of the 6 ductal adenocarcinomas and in one neuroendocrine tumor [5]. While negative for HP, a high sequence similarity to *Helicobacter pullorum* could be found in one sample.

While we agree with Manes *et al.* [1] that the exact role of HP in pancreatic cancer has not been elucidated in detail as opposed to the development of gastric cancer or gastric mucosa-associated lymphoid tissue (MALT) lymphoma, these two studies demonstrate at least an association between HP carriage and the risk of pancreatic cancer. In addition, the data from Nilsson *et al.* [5] suggest that other *Helicobacter* species might be involved, and that serologic findings with antibodies against HP might, in fact, be cross-reactive. In view of the dismal prognosis of the disease, further

additional work is warranted to identify the exact *Helicobacter* species involved as well as the role of the bacteria in the carcinogenesis of pancreatic cancer. This might be of potential impact for the identification of preventive approaches such as antibiotic eradication, as are currently being studied in gastric cancer.

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Keywords Carcinogens; Gram-Negative Bacteria; *Helicobacter*; *Helicobacter pylori*; Lymphoma, Mucosa-Associated Lymphoid Tissue; Organisms Category; Pancreatic Diseases; Pancreatic Neoplasms; Risk Factors

Abbreviations HP: *Helicobacter pylori*; MALT; mucosa-associated lymphoid tissue

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REPLY

Dear Sir:

We thank Dr. Wöhrer and colleagues for their comments [1] on our review article [2] on *Helicobacter pylori* and the pancreas. The connection between the bacterial infection and pancreatic cancer could become an intriguing field of research. The epidemiological data which exist today are the only such data which support the reliability of this association. The mechanisms by which a chronic *Helicobacter pylori* infection may favour the onset of pancreatic cancer as well as the fact that curing the infection may reduce the occurrence of the disease in high risk patients (patients with chronic pancreatitis for example) should be the object of further investigations.

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