already have comparable levels of Cox-2 expression to GC and can therefore be regarded as precancerous lesions.

**4003**

**SP Expressing Metaplasia (SPEM) and Early Gastric Cancer**

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BACKGROUND Although the association of H. pylori with gastric adenocarcinoma is now well established, the mechanism by which chronic H. pylori infection contributes to gastric adenocarcinoma is poorly understood. Recently, a novel metaplastic cell lineage in the body mucosa was described, which has morphological similarities to Brunners glands and expresses the trefoil peptide spasmolytic polypeptide (SP). Designated SPEM (SP expressing metaplasia), this lineage was strongly associated with both chronic H. pylori infection and gastric adenocarcinoma. This study investigated the association between early gastric adenocarcinoma and SPEM. METHODS Twenty-nine patients with early gastric cancer diagnosed in the years 1983 to 2000 who had archival tissues from gastric resections, were found in databases provided by the Surgical and Pathology Departments of the Icelandic University Hospital. For each case, six sections were selected (two containing cancer, the others without), recut and stained with H&E, PAS-DIA, and gastrin plus SP immunostaining. These histological sections were examined and the results analysed. The presence of SPEM and IM adjacent to and distant from the cancer was compared and SP immunostaining within dysplastic/cancerous cells was investigated. RESULTS Sixteen early gastric cancers were located in the antrum, three in the vicinity of the cancer. In 76% of all the twenty-nine cases, SPEM was present in the body mucosa distant from the cancer and was usually associated with atrophic gastritis. On the other hand, IM was found adjacent to the tumor in 76% of cases and in body sections in 52% of resections. SP immunostaining was noted within cancer cells in 62% of tumors, and within dysplastic cells in 78% of resections where dysplasia was present. The SP positivity was almost always located in the deepest portions of the dysplastic/cancerous glands and (sub)apically in the cells. CONCLUSION These results support the hypothesis that SPEM is associated with gastric cancer. High levels of SP staining in dysplastic and neoplastic cells associated with early gastric cancers suggests that SPEM may be a precursor to the evolution of dysplasia and adenocarcinoma in gastric mucosa infected with H. pylori.

**4004**

**Expression of the DNA Repair Enzyme Apurinic/Apyrimidinic Endonuclease in Gastric Mucosa and the Effect of Helicobacter pylori Infection.**

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Introduction: The multi-function enzyme apurinic/apyrimidinic endonuclease (APE) regulates a number of transcription factors including NF-kB, AP-1 and p53 and is essential in DNA base excision repair. Patterns of expression are altered in cervical and ovarian cancers and APE is upregulated by oxidative stress. This has recently been demonstrated in gastric cancer cell lines, suggesting that upregulation in vivo may limit oxidative DNA damage induced by H. pylori. Our aim, therefore, was to determine the effect of H. pylori infection on expression of APE in gastric biopsies. Methods: At endoscopy, antral and corpus biopsies were taken from 36 patients (mean age 51 years, range 19-70) who had not been taking proton pump inhibitors or NSAIDs. H. pylori infection was determined by histology and urease testing. APE mRNA and G3PDH mRNA (control) were analysed by semi-quantitative RT-PCR and computer image analysis. Presence of APE protein was determined immunohistochemically in formalin fixed gastric biopsies using a mouse monoclonal antibody against APE. Results: APE mRNA of the cDNA was similar in antral biopsies from H.pylori positive (1.02, SEM 0.24) and negative (0.98, SEM 0.23) patients (p = 0.95). SEM of 0.16 -0.73. APE mRNA expression was observed in all but 3 antral biopsies and in all corpus biopsies. Expression of APE/G3PDH was higher in the corpus (0.76, SEM 0.13) than antrum (0.42, SEM 0.10) but this did not reach statistical significance (p = 0.09, 95%CI of difference -0.60 to 0.05, n = 15). Immunohistochemistry of infected and uninfected biopsies demonstrated APE expression in virtually all fooreal and glandular epithelial cells, with relative sparing of the superficial mucosa. Staining was predominantly nuclear although cytoplasmic staining was also seen, mainly in the glandular epithelium. Conclusions: Although H. pylori increases oxidative stress in the gastric mucosa, the DNA repair enzyme APE is not upregulated in infected samples. APE mRNA and protein are expressed constitutively in gastric epithelial cells. This study was funded by a grant from Yorkshire Cancer Research.

**4005**

**Long Term Infection With Helicobacter Pylori Induces Intestinal Metaplasia, Carcinized And Cancer In The Stomachs Of Mongolian Gerbils. Effect Of Eradication.**

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Watanabe et al. 1999 reported that H. pylori induced gastric carcinoid and cancer 62 wk after infection in Mongolian gerbils (M. gerbils). In this study, we examined whether eradication of H. pylori can prevent the development of gastric adenocarcinoma. After 2000 who had archival tissues from gastric resections, were found in databases provided by the Surgical and Pathology Departments of the Icelandic University Hospital. For each case, six sections were selected (two containing cancer, the others without), recut and stained with H&E, PAS-DIA, and gastrin plus SP immunostaining. These histological sections were examined and the results analysed. The presence of SPEM and IM adjacent to and distant from the cancer was compared and SP immunostaining within dysplastic/cancerous cells was investigated. RESULTS Sixteen early gastric cancers were located in the antrum, three in the vicinity of the cancer. In 76% of all the twenty-nine cases, SPEM was present in the body mucosa distant from the cancer and was usually associated with atrophic gastritis. On the other hand, IM was found adjacent to the tumor in 76% of cases and in body sections in 52% of resections. SP immunostaining was noted within cancer cells in 62% of tumors, and within dysplastic cells in 78% of resections where dysplasia was present. The SP positivity was almost always located in the deepest portions of the dysplastic/cancerous glands and (sub)apically in the cells. CONCLUSION These results support the hypothesis that SPEM is associated with gastric cancer. High levels of SP staining in dysplastic and neoplastic cells associated with early gastric cancers suggests that SPEM may be a precursor to the evolution of dysplasia and adenocarcinoma in gastric mucosa infected with H. pylori.

**4006**

**Analysis of p53 Mutations and Helicobacter pylori Infection in Human and Animal Models.**

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BACKGROUND: It is considered that p53 gene mutations play a critical role in the development of gastric carcinomas. We examined the relationship between Helicobacter pylori (H. pylori) infection and p53 gene mutation of gastric mucosa in human and animal models. Methods: To detect original p53 DNA sequence of Japanese monkey and Mongolian gerbil, p53 gene of 20 animals were amplified using nested PCR method with the primers for human p53 gene. Direct DNA sequencing of exons 5, 6, 7, and 8 of the p53 genes were performed by dyeodeoxy terminator method for gastric mucosa of human, Japanese monkey and Mongolian gerbil. Expression of p53 was examined immunohistochemically in Japanese monkey model. Results: Mutations in p53 gene were identified in 30% of gastric samples of H. pylori positive (H. pylori) infection and p53 gene mutation of gastric mucosa in human and animal models. No mutations were identified in 20% of gastric samples of H. pylori negative (H. pylori) infection and p53 gene mutation of gastric mucosa in human and animal models. Conclusion: These findings demonstrate that the H. pylori infection can induce p53 point mutations in human and Japanese monkey and appear to be involved in the pathway leading to dysplasia or carcinoma. However, there was no p53 mutation in Mongolian gerbil model at present in our Direct DNA sequencing method, further studies about this model are needed.

**4007**

**The Mongolian Gerbil Gastric Epithelial Cell Line Immortalized by SV-40 Large T Antigen.**

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Background: Helicobacter pylori has been assumed as a gastric carcinogen in human. To investigate the molecular mechanism of gastric carcinogenesis by H. pylori, we in vitro system to investigate the interaction between the bacteria and the host gastric epithelial cells is crucial. So far, H. pylori infection without any carcinogen has been shown to cause the gastric adenocarcinoma only in the Mongolian gerbil as an animal model. Aim: To make an immortalized gastric epithelial cell line from the Mongolian gerbil, which is an H. pylori positive (H. pylori) infection and p53 gene mutation of gastric mucosa infected with H. pylori, specifically in the neck region of the glands. Conclusions: These findings demonstrate that the H. pylori infection can induce p53 point mutations in human and Japanese monkey and appear to be involved in the pathway leading to dysplasia or carcinoma. However, there was no p53 mutation in Mongolian gerbil model at present in our Direct DNA sequencing method, further studies about this model are needed.