ΞΕΝΟΓΛΩΣΣΕΣ ΑΝΑΚΟΙΝΩΣΕΙΣ
(ABSTRACTS)
ΕΛΛΗΝΩΝ ΕΡΕΥΝΗΤΩΝ

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Helicobacter pylori infection and duodenogastric reflux (DG.R.)

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Objective. H.p. infection and DG.R. are linked with chronic gastritis, intestinal metaplasia and dysplasia. The relationship between H.p. infection and DG.R. is, as yet, unclear. The objective of this study is to investigate any possible link between them.

Methods. 101 patients (comprising 53 men and 48 women), median age 57 years (range 21–86) underwent gastroscopy, because of epigastric discomfort. None of them had history of cholecystectomy or diseases of the bile duct. They were separated into two groups. The first group comprised of 46 patients, were diagnosed with DG.R. The second comprised of 55 patients, were not diagnosed with DG.R. The methods of diagnosis used for H.p. infection, were firstly by histological examination, and secondly by rapid urease test. The statistical analysis took place under X^2 test control conditions. These, were confirmed by applying the model of logistical regression.

Results. From the group of patients diagnosed with DG.R., 28 (60.8%) proved to be H.p. (+) and 18 (39.2%) H.p. (–). From the group of patients who were not diagnosed with DG.R., 30 (54.5%) proved to be H.p. (+) and 25 (45.5%) H.p. (–). The percentage of H.p. infection was not higher in patients who were diagnosed with DG.R., than those who were not ($p > 0.05$). In addition, there was no difference between male and female results.

Conclusions. This study did not find any connection between DG.R. and H.p.

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Helicobacter pylori (Hp) increases matrilysin (MMP-7) expression in gastric epithelial cells in a Cag dependent manner in the antrum but not in the cardia

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It is reported that Hp up-regulates MMP-7 expression in the epithelium of antrum (A) and fundus (F) and that this expression is more intense in Cag(+) Hp strains. It was suggested that this expression could be related to carcinogenesis. The aim of our study was to determine if this up-regulation is also observed in the cardia (C).

Patients and methods. 76 patients (38 men), 47 Hp(+), 31 CagA(+) were enrolled in the study. All patients were not taking NSAID's for at least one month. Biopsies from A, F and C were obtained. Anti-CagA status was assessed by ELISA.

All biopsies were stained with May Grunwald Giemsa. Immunohistochemistry was performed with monoclonal antibody [MMP-7, Ab1(Clone 1D2)]. Slides were assessed blindly for intensity in the proliferative zone (0: none, 1: mild, 2: moderate, 3: very intense).

Results. Mean age ± SD: 45.3 ± 12.1. MMP-7 intensity assessment is shown in the table. In each cell corresponds the absolute number of patients for a degree of intensity in an order of 0/1/2/3.

Conclusions. (1) The presence of Hp increases MMP-7 expression in A and F (2) CagA(+) strains increases MMP-7 expression in the A but not in the F compared to the CagA(–) and (3) Neither Hp nor CagA influence MMP-7 expression in the cardia.

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Helicobacter pylori colonization in palatine salivary glands

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Introduction. Recently, a case of MALT lymphoma of the parotid gland in Sjögren's syndrome associated with localized *Helicobacter pylori* (HP) infection was described. Furthermore, it has found that HP can bind to salivary mucins, mainly those that are secreted from the palatine salivary glands because of higher degree of sulfation. However, there is no report whether this microorganism might colonize the palatine salivary glands of the oral cavity.

Aim. To investigate by immunohistochemistry the HP status of palatine salivary glands.

Material and method. Formalin-fixed, paraffin-embedded tissue blocks of palatine mucosa containing palatine salivary glands from tonsillectomy specimens for tonsillitis (26 cases) were studied. All sections were stained using hematoxylin & eosin for histologic examination and a polyclonal antibody for HP using an immunoperoxidase technique following heat induced antigen retrieval.

Results. Microscopically, no pathologic changes were detected in palatine salivary glands. Immunohistochemically, no distinct bacillary structures (helical and/or coccoid forms) were detected neither in the acini nor in the salivary duct system. However, anti-HP antibody showed immunoreactivity with acinar system antigens. Specifically, they recognized the cytoplasm of mucous acinar cells in most palatine salivary glands sections.

Conclusions. Antibody reactivity of cells in the acini of the palatine salivary glands may either be due to internalization of HP by these cells, or to cross-reactivity of anti-HP IgG with epithelial cell epitopes. The too high rates of positive reaction make the second explanation more likely, supporting the theory of an autoimmune reaction induced by HP infection.

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Aspirin Influences Matrilysin (mmp-7) Expression in Gastric Epithelial Cells

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Introduction. *Helicobacter pylori* [Hp] up-regulates matrix metalloproteinase-7 [MMP-7] expression in the gastric epithelium. This expression is more intense in CagA(+) Hp strains. It is suggested that this could be related to carcinogenesis

Aims and methods. To examine if chronic aspirin intake influences that up-regulation, 142 patients (81 men) were enrolled in the study Group I: 81 patients without aspirin consumption - 52Hp(+), 36CagA(+) and Group II: 61 patients - 36Hp(+), 24CagA(+) taking 100–500 mg/day of aspirin for more than 2 months. Anti-CagA status was assessed by ELISA. Immunohistochemistry was performed on paraffin embedded gastric biopsy samples using a mouse monoclonal anti-MMP-7 antibody (Clone ID2-NeoMarkers) MMP-7 staining intensity in epithelial cells of the proliferative zone of the gastric mucosa was graded blindly (0: none, 1: mild, 2: moderate, 3: very intense – cytoplasmic expression).

Results. Mean age ± SD: 44.9 ± 12.8. MMP-7 intensity assessment is shown in the table. In each cell the absolute number of patients for the corresponding staining intensity score is shown in an order of 0/1/2/3

	Antrum	p	Antrum + Asp	Fundus	p	Fundus + Asp
Hp(-)	19/7/3/0	*	10/3/4/8	25/4/0/0	*	12/12/1/0
p	*		NS	*		NS
Hp(+)CagA(–)	5/6/3/2	NS	2/4/4/2	6/8/1/1	NS	4/3/2/3
p	**		NS	NS		NS
Hp(+)CagA(+)	2/8/10/16	NS	3/1/11/9	13/11/8/4	NS	12/7/3/2

*$p < 0.05$ between Hp(+) and Hp(–) of the same topographic distribution of each Group. **$p < 0.05$ between CagA(+) and CagA(–). ³$p < 0.05$ between patients taking and not taking aspirin.

Conclusion. (1) Hp infection enhances MMP-7 gastric epithelial expression in a CagA dependent manner (2) Aspirin increases MMP-7 expression in Hp(–) both in antral and fundic mucosa.

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Microsatellite instability (MSI) in chromosome 17: A molecular and tissue microarrays study in gastric carcinogenesis (GC) – Correlation with *Helicobacter pylori* (Hp) infection

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Introduction. Genomic instability may be an early event in carcinogenesis.

Aim. We studied chromosome 17 MSI to elucidate the role of Hp in the GC pathway.

Material methods. 45 carcinomas (25Hp+ and 20Hp–) were studied for determination of MSI. 12Hp+ and 10Hp– carcinomas were classified as diffuse, whereas 13Hp+ and 10Hp– as intestinal type. In Hp+ cases, intestinal metaplasia (IM) I observed in 5, II in 8 and III in 12 cases. Controls (Hp–) included 5 IM I, 6 IM II, 10 IM III. The TMArrayer apparatus was used for construction of TMAs. DNA obtained from TMA gastric specimens, amplified with 2 microsatellites markers (D17S250, TP53DNA) and properly analyzed.

Results. 10/13 of intestinal and 6/12 of diffuse Hp+ carcinomas were expressed MSI, as well as 0/5 IM I, 3/12 IM II and 7/8 IM III Hp+ cases. Three Hp– of diffuse and 5Hp– of intestinal carcinomas were also revealed MSI, whereas MSI was expressed in 0/5 of IM I, 1/6 of IM II and 4/10 of IM III Hp– cases. IM and carcinoma MSI-positive cases were also analyzed by chromogenic in situ hybridization. Aneuploidy was observed in 9/13Hp+ carcinomas of intestinal, in 4/12 Hp+ of diffuse type as well as in 2/12Hp + IM II and in 6/8Hp+ IM III cases. In contrary, 2/10Hp– IM III cases revealed chromosome 17 aneuploidy.

Conclusions. Results indicate an involvement of MSI in Hp infected gastric cells that have entered the multistep GC pathway, through mechanisms involving activation of chomosome 17-related oncogenes, aneuploidy and deregulation of cell cycle.

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Cytomegalovirus (CMV) as a possible factor in pathogenesis of gastric cancer and its relationship with *Helicobacter pylori*

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Aim. Estimation of possible role of CMV, alone or correlated with HP, in the pathogenesis of gastric adenocarcinoma.

80 nonimmunocompromised patients (gastric cancer: 40-premalignant lesions: 40) and 80 individuals with nonendoscopic evident gastric disease (control group), were enrolled in the study. Bioptic specimens were obtained from the malignant-premalignant lesions, 3 cm away from the lesions and from endoscopically healthy mucosa from the patients and the control group. Polymerase chain reaction (PCR) was used to identify the CMV genome. The presence of HP was investigated with CLO-test and histological examination of mucosal gastric samples from the antrum and/or the corpus of the stomach. Multivariate statistical analysis correlated the results with epidemiological parameters which may be involved in the disease's pathogenesis.

The viral genome was detected in 11/40 (27.5%) tissue samples from malignant lesions, 15/40 (37.5%) samples from premalignant lesions, but in none of the bioptic specimens from endoscopically healthy mucosa either from patients or control group. HP was detected in 15/40 (37.5%), 24/40 (60%), 37/80 (46.2%) of each group. χ^2-statistical analysis revealed significant difference in the detection rate between the control population and the two patients' groups ($p < 0.001$). No-significant statistical correlation was observed between the detection rate of viral genome and the detection rate of HP in the two examined patients' groups ($p = 0.999$, $p = 0.317$, respectively) and between the detection rate of CMV and the epidemiological parameters involved in gastric carcinogenesis. No-statistically significant difference was noted between the detection rates of HP of the two patients' groups ($p = 0.074$).

Our results indicate a possible role of CMV in gastric adenocarcinoma pathogenesis as independent factor in a patients' subgroup.

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Effective single agent chemotherapy in patients with low grade gastric and duodenal lymphoma after failure of anti-*Helicobacter pylori* (HP) therapy

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Background. Almost 70% of gastric low-grade (LG) mucosa-associated-lymphoid-tissue-(MALT) lymphomas (NHL) show complete response (CR) to the anti-HP treatment. Patients with recurrent or progressive disease, despite HP eradication, are candidates for chemotherapy.

Aim. To present the outcome of 2 patients with LG/MALT/NHL who relapsed or failed to respond despite successful HP eradication.

Patients. A 71 y man with multiple hepatic echinococcal cysts since 1992, underwent gastroscopy (6/1996) because of epigastric discomfort. Endoscopy showed extensive nodular/ulcerated gastric mucosal folds. Histology/staging revealed a IIEA, LG/MALT(CD20+, MIB1 staining < 7%) & HP infection grade II. The patient received classical OACx14 days. Complete reevaluation (gastroscopy-biopsies, ^{13}C-UBT) documented HP eradication. Because no signs of endoscopic/histologic NHL regression were seen in the next 6 month, he received second-line chlorambucil 7.5 mg/day po × 6 month without toxicity. CR was documented for 2 years when gastroscopy/biopsies & an endoscopic ultrasound (EUS) revealed relapse of LG/MALT causing circumferential stenosis of the gastric antrum but no HP recrudescence. The patient retreated with chlorambucil 7.5 mg/day × 10 months & achieved pCR, sustained until now.

A 37 y woman presenting in 7/2002 with epigastric pain, indigestion & bloating, underwent gastroscopy/biopsies, EUS & barium meal which revealed an ulcerated polypoid mass 4 × 5 cm at the apex of the duodenal bulb. Histology/staging revealed a IIEA, LG/MALT marginal zone (CD5+, CD20+, proliferation rate < 10%) & HP infection/gastritis gradeIII. She received OACx14 days without NHL response, despite HP eradication. Then, she was taken chlorambucil 7.5 mg/day × 12 months po, without toxicity & is in pCR for 16 + mo.

Conclusion. Patients with upper GI LG/MALT/NHL associated with HP infection, unsuccessfully treated with anti-HP regimens, may undergo CR with chlorambucil po, without any toxicity.

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Abstract no. 08.06

Effect of *H. pylori* eradication on esophageal acid exposure and oesophageal motility in patients with Gastroesophageal Reflux Disease (GERD)

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Aim and methods. To investigate the impact of *Helicobacter pylori* eradication on the oesophageal acid exposure and esophageal motility in patients with GERD. Thirty-seven patients (M:25, W12, mean age 42 years, range 19–65) with GERD Hp(+) underwent endoscopy-biopsy, manometry and 24-h pH-metry. All patients received standard eradication treatment, and they were re-examined with pH-metry, manometry, endoscopy-biopsy. The statistical analysis was made with ANOVA and Pearson tests.

Results. Pre-treatment endoscopy showed reflux oesophagitis in 18 patients (Savary Miller grade 1:14, 2:4) and Negative Endoscopy Reflux Disease (NERD) in 19. All patients had antrum predominant gastritis. The mean De Meester score was 47.1. The mean Lower Oesophageal Sphincter Pressure (LOSP) was 13.2 mmHg. The motility of the esophageal body was normal in 33 patients (all NERD and grade 1 oesophagitis). The 4 patients with grade 2 oesophagitis had ineffective motility of oesophageal body and LOSP < 7 mmHg. After successful Hp eradication both gastritis and oesophagitis were healed in all patients. The mean De Meester score after eradication was 14.2, a significant decrease compared to the pretreatment score ($p < 0.001$). After eradication a slight increase in LOSP (14.2 mmHg) was observed (NS). In the 4 patients with grade 2 oesophagitis and ineffective motility the oesophageal corpus activity returned to normal with no change in LOSP.

Conclusions. 1. The eradication of Hp infection may lead to a decrease in gastrooesophageal reflux, and may have no effect on LOSP and oesophageal body motor activity. 2. The type of gastritis of our patients may have influenced the results.

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Combination Of Rapid Urease Test With Rapid Serology Test For The Early Detection Of *Helicobacter pylori* Infection In Patients With Bleeding Duodenal Ulcers

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The sensitivity and negative predictive value (NPV) of the rapid urease test (RUT) is lower in patients with active ulcer bleeding (AUB). The combined efficacy of a RUT and a rapid whole blood antibody test (WBA) has not been established in these patients. Aim of this study was to evaluate the combined efficacy of a RUT and a WBA test in patients with AUB. HP infection was determined by the Assure test (WBA), *H. pylori* rapid test (Alpha Medical), CLO test and histology. The HP load in histology was graded from 1: low HP load up to 3: high HP load. 30 patients with bleeding and 11 with nonbleeding DUs at endoscopy were studied. The prevalence of HP in bleeders was 83% compared to 91% in nonbleeders, as defined by histology. Both RUT and WBA test did not differ significantly in sensitivity, specificity, positive and NPV, both in cases and controls. In patients with AUB, when the HP load was low (grade 1 and 2), the difference in sensitivity of RUT vs. WBA fell just short of significance (0.36 vs. 0.55, $p = 0.04$). The sensitivity and NPV of the combination was 0.84 and 0.43, respectively. The kappa of agreement of their combination, compared to histology, was significant both in patients (0.37, $p = 0.034$) and controls. That was not observed for each test independently. In patients with aub: 1. RUT significantly lacks sensitivity, compared to WBA, when HP load is low. 2. The combination of both tests is more accurate for the diagnosis of HP infection.

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Do hyperplastic polyps of the colorectum represent an extragastric reservoir for *Helicobacter pylori* infection?

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Introduction. Recent studies have demonstrated the bidirectional differentiation of the hyperplastic polyps of the colorectum to both gastric foveolar and colonic epithelial cells in the same crypt. This finding in combination with their malignant potential as has been suggested in several recent important studies, raises the question of whether *Helicobacter pylori* (HP) is settling in the colorectal hyperplastic polyps.

Material and method. A retrospective study. A total of 25 hyperplastic polyps of the colorectum, which were endoscopically or surgically resected were investigated. Immunohistochemical analysis was carried out on formalin-fixed paraffin-embedded 4-μm sections using a polyclonal antibody directed against HP using an immunoperoxidase technique following heat induced antigen retrieval.

Results. HP was present in 8 of the 26 polypectomy specimens (26,92%). In HP positive cases, both helical and coccoid forms were found in high numbers, in the superficial mucous layer, attached to the columnar cells with clear cytoplasm and small oval nuclei, resembling gastric foveolar epithelial cells.

Conclusions. Our research suggests that hyperplastic polyps of the colorectum may be an ecological niche for HP. To our knowledge, this is the first documented study by immunohistochemistry on detection of HP in hyperplastic polyps of the colorectum.

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Effect of Lactic Acid Bacteria on gastric inflammation and humoral immune response towards *H. pylori* in the SS1 mouse infection model

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We have evaluated the effect of individual lactobacilli (LAB) belonging to different species (*L. johnsonii* La1, L. amylovorus DCE 471 and L. acidophilus IBB 801) for their potential ability to affect *H. pylori* (Hp) colonization and the associated gastritis in C57BL/6 mice infected by the Hp SS1 strain.

We administered LAB continuously through the animal drinking water and found that a daily dose of 10^8 cfu/animal did not eradicate or reduce Hp colonization at 6 and 12 weeks post-infection, as assessed by viable cultures. However, there was a significant reduction in chronic inflammation (updated Sydney system) at 6 weeks ($p = 0.003$, Wilcoxon rank sum test) and 12 weeks ($p = 0.038$) in the La1-treated animals compared to Hp-infected controls, but only at 6 weeks postinfection in the two other LAB-treated groups (DCE 471 $p = 0.047$ and IBB 801 $p = 0.014$). Moreover, in all the LAB-treated animals, we observed a striking attenuation of chronic active gastritis, as a significantly reduced number of neutrophils invaded the lamina propria, throughout the whole 12-week period (La1 $p = 0.003$, DCE 471 $p = 0.011$ and IBB 801 $p = 0.011$). Anti-Hp IgG antibodies in the serum were depressed significantly only in the case of La1-treated Hp-infected animals ($p < 0.05$, Students t-test), although a tendency for reduction in antibody titers was also observed in the other two LAB-treated animal groups. These results point out that factors either secreted by or expressed on live LAB can influence both the anti-Hp humoral response and the neutrophilic infiltration in the lamina propria, a hallmark of *H. pylori* infection.

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Helicobacter pylori (Hp) Seropositivity influences the time of starting as well as the frequency of Vomiting in pregnancy

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The role of Hp in vomiting during pregnancy is not well established.
Aim. To investigate the relationship of Hp with the presence and the pattern of vomiting Patients and methods: 221 pregnant women have completed a questionnaire the day after their delivery about the frequency and duration of vomiting during their pregnancy. A serology for Hp (ELISA) and CagA was performed.
Results. Age 26.2 ± 5.5 years, 54.1% had vomiting during their pregnancy. Cp (+) prevalence was 59.4%, CagA seropositivity 78.3%.

Mean duration of vomiting. 10.0 ± 6.9 (1–35) weeks. Mean time of starting vomiting: 4.6 ± 5.6 (1–38) weeks. No correlation between Hp (+) or CagA (+) and vomits or its duration. Hp seropositivity was correlated to the time of starting vomiting [5.5 ± 6.3 weeks for Hp (-) vs. 3.5 ± 3.1 weeks for Hp(+), $p < 0.05$] but was not for CagA (+). The mean number of vomits per day was higher in Hp (+) women mainly at the beginning and the end of the vomiting period (Pillai's Trace = 0.10, $p < 0.01$), mainly for the 1st (0.75 ± 1.45 vs. 0.54 ± 1.09) and the 5th month (0.34 ± 1.23 vs. 0.17 ± 0.65). Age, BMI, prior gestations, and the titles of anti-Hp and anti-CagA were not significant.
Conclusions. (1) Hp seropositivity was not related to the presence of vomits in pregnancy (2) Starting of vomiting is observed earlier, while the daily frequency of vomits tends to be higher in Hp (–) women, mainly in the beginning and the end of the vomiting period (3) CagA seropositivity does not influence the presence or seriousness of vomiting.

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CAGA POSITIVE HELICOBACTER PYLORI STRAINS ARE ASSOCIATED WITH INCREASED RISK OF PEPTIC ULCER BLEEDING AMONG NSAID USERS. A MULTICENTER CASE-CONTROL STUDY

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INTRODUCTION: The role of Helicobacter pylori infection and especially of the cytotoxin associated gene product strain in peptic ulcer bleeding among chronic NSAIDs users remains controversial.
AIMS & METHODS: A case-control study was carried out of 191 consecutive chronic NSAIDs users admitted because of peptic ulcer bleeding. Peptic ulcer was verified by endoscopy. Controls were 196 chronic NSAIDs users without signs of bleeding of similar age and gender as cases. Multivariate regression analysis was performed for further evaluation of the interaction among H. pylori, CagA status and other risks factors.
RESULTS: H. pylori infection was present in 121 (63.4%) cases compared with 119 (60.7%) controls (OR=1.14, 95%CI, 0.76-1.72). CagA positive strains were found to be significantly more frequent in cases than controls (65/106 versus 41/99 p=0.008). Current smoking (OR=2.65, 95%CI 1.14-6.15, p=0.02) CagA status (OR=2.28; 95%CI, 1.24-4.19; p=0.008), dyspepsia (OR=6.89; 95%CI, 1.84-25.76, p=0.004) and past history of peptic ulcer disease (OR=3.15, 95%CI, 1.43-6.92; p=0.004) were associated significantly with increased risk of bleeding peptic ulcer.
CONCLUSION: Results suggest that CagA - positive H. pylori infection is associated with a more than 2-fold increased risk of bleeding peptic ulcer among chronic NSAIDs users.

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ASPIRIN INFLUENCES MATRILYSIN (MMP-7) EXPRESSION IN GASTRIC EPITHELIAL CELLS

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INTRODUCTION: Helicobacter pylori (Hp) upregulates matrix metalloproteinase-7 (MMP-7) expression in the gastric epithelium. This expression is more intense in CagA(+) Hp strains and it is suggested that this could be related to carcinogenesis.
AIMS & METHODS: The aim of our study was to examine if chronic aspirin intake influences this upregulation. Patients and methods: 142 patients (81 men) were enrolled in the study. Group I. 81 patients without aspirin consumption - 52Hp(+), 36 CagA(+) and Group II. 61 patients - 36Hp(+), 24 CagA(+) taking 100-500 mg/day of aspirin for more than 2 months. Anti-CagA status was assessed by ELISA. Immunohistochemistry was performed on paraffin embedded gastric biopsy samples using a mouse monoclonal anti-MMP-7 antibody (Clone ID2-NeoMarkers). MMP-7 staining intensity in epithelial cells of the proliferative zone of the gastric mucosa was graded blindly (0: none, 1: mild, 2: moderate, 3: very intense - cytoplasmic expression).
RESULTS: Mean age±SD:44.9±12.8. MMP-7 intensity assessment is shown in the table. In each cell the absolute number of patients for the corresponding staining intensity score is shown in an order of 0/1/2/3.

	Antrum	p	Antrum+As	Fundus	p	Fundus+As
Hp(-)	19/7/3/0	$	10/3/4/8	25/4/0/0	$	12/12/1/0
p	*		NS	*		NS
Hp(+)CagA(-)	5/5/3/2	NS	2/4/4/2	8/6/1/1	NS	6/3/2/1
p	**		NS	NS		NS
Hp(+)CagA(+)	2/8/10/16	NS	3/7/11/5	13/11/8/4	NS	12/7/3/2

*p<0.05 between Hp(+) and Hp(-) of the same topographic distribution of each Group, ** p<0.05 between Cag A (+) and CagA (-), $ p< 0.05 between patients taking and not taking aspirin.
CONCLUSION: 1) Hp infection enhances MMP-7 gastric epithelial expression in a CagA dependent manner, 2) Aspirin increases MMP-7 expression in Hp(-) both in antral and fundic mucosa. This observation is probably not correlated to gastric carcinogenesis but it may be related to an increased activity of MMP-7 for the cleavage of the induced by aspirin membrane-bound TNF-alpha. 3) MMP-7 gastric epithelial expression should be carefully interpreted in patients taking aspirin, when evaluated in the carcinogenic process.

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IS HELICOBACTER PYLORI ERADICATION THE TREATMENT OF CHOICE FOR PEPTIC ULCER DISEASE IN PATIENTS WITH LIVER CIRRHOSIS?

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INTRODUCTION: Helicobacter pylori eradication is the standard treatment to cure peptic ulcer disease. The role of H. pylori in peptic ulcer in patients with liver cirrhosis has not been studied
AIMS & METHODS: To investigate the natural course of peptic ulcer disease in cirrhotics, after healing with either H. pylori eradication or omeprazole (OME) therapy.
Consecutive patients with liver cirrhosis and peptic ulcer were studied. Patients had never received H. pylori eradication and had not used NSAIDs or proton pump inhibitors the past two months before entering the study. All underwent endoscopy at entry with H. pylori testing (histology). Helicobacter pylori +ve patients received one week triple eradication therapy followed by 20 mg/d OME for three weeks, and H. pylori -ve patients were treated with 20 mg/d OME for four weeks. Follow up endoscopies were performed four weeks after completion of therapy and at 12 and 24 months or when symptoms recurred. Those patients with ulcer recurrence were treated with 20 mg/d OME maintenance therapy.
RESULTS: Out of 28 patients (24 male, 4 female, aged 61, 48-71 years, 18 alcoholics, 10 non-alcoholics, Child: A=13, B=10, C=5), 18 had a duodenal and 10 a gastric ulcer. In 17/18 H. pylori +ve patients H. pylori was successfully eradicated. All ulcers were healed at 4 weeks after eradication or OME therapy. During the 24 months follow up period ulcer relapsed in 17 (8/18 H. pylori +ve, 9/10 H. pylori -ve, p=0.041) out of the 28 patients. There was no ulcer relapse while on OME maintenance therapy. Multivariate regression analysis showed that a negative H. pylori status at entry to the study (x2=11.4, p<0.001), older age (x2=7.7, p=0.005) and the severity of cirrhosis (Child) (x2=4.8, p<0.03) were significantly related to ulcer recurrence. Sex, etiology of cirrhosis and type of ulcer were rejected by the model
CONCLUSION: Helicobacter pylori eradication does not protect H. pylori +ve cirrhotics from ulcer recurrence. Therefore, omeprazole maintenance treatment is mandatory, irrespectively of H. pylori status.

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MICROSATELLITE INSTABILITY IN CHROMOSOME 17: A MOLECULAR AND TISSUE MICROARRAYS STUDY IN GASTRIC CARCINOGENESIS - CORRELATION WITH HELICOBACTER PYLORI (HP) INFECTION

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INTRODUCTION: The role of microsatellite instability (MSI), a form of genomic abnormality expressed mainly in tumors, remains unknown. MSI is identified when alleles of novel sizes are detected in microsatellites sequences derived from cancer DNA that are not present in normal tissues of the same individual. Recent studies tried to determine the implication of MSI in the initiation of gastric carcinogenesis, suggest that genomic instability may be an early event in this multistep procedure.

AIMS & METHODS: We analyzed chromosome 17 MSI by TMA method, in preneoplastic and gastric carcinoma cases after Hp infection, in order to elucidate the possible role of Hp in the gastric carcinogenesis pathway. 45 formalin fixed, paraffin embedded gastric carcinoma cases taken from the archives of 417 VA Hospital were studied for determination of MSI (25 Hp+ and 20 Hp-). 12 Hp+ and 10 Hp- carcinomas were histologically classified as diffuse and 13 Hp+ and 10 Hp- as intestinal type (according to Lauren). Intestinal metaplasia (IM) type I were observed in 5 Hp+ cases, IM II in 6 and IM III in 12 of them. Controls included 5 Hp- IM I, 6 IM II and 10 IM III cases. The TMArrayer apparatus (Chemicon, USA) was used for the construction of TMAs. DNA obtained from TMA gastric specimens was amplified with a set of 2 microsatellites markers (D17S250 and TP53DNA) and properly analyzed.

RESULTS: 10/13 of intestinal and 6/12 of diffuse Hp+ gastric carcinomas were expressed MSI in chromosome 17, as well as 0/5 Hp+ IM I, 3/12 IM II and 7/8 IM III. Three Hp- of diffuse and 5 Hp- of intestinal carcinoma cases were also revealed MSI. Furthermore, MSI was expressed in 0/5 of IM I, 1/6 of IM II and 4/10 of IM III Hp- cases. IM and carcinoma MSI-positive cases were also analyzed by chromogenic in situ hybridization (CISH, Zymed, USA). Aneuploidy were observed in 9/13 Hp+ carcinomas of intestinal, in 4/12 Hp+ of diffuse type as well as in 2/12 Hp+ IM II and in 6/8 Hp+ IM III cases. In contrary, 2/10 Hp- IM III cases revealed chromosome 17 aneuploidy.

CONCLUSION: Our data suggest a significant correlation between chromosomal 17 abnormalities and initiation of gastric carcinogenesis after Hp infection. The results indicate an early involvement and continuous accumulation of MSI in Hp-infected gastric cells that have entered the multistep gastric carcinogenesis pathway, mainly through mechanisms involving activation of chomosome 17-related oncogenes, aneuploidy and finally deregulation of cell cycle.

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IN SITU H. PYLORI INFECTION AND ONCOGENES' EXPRESSION IN PATIENTS WITH COLORECTAL CANCER

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INTRODUCTION: H. pylori infection has been classified by the WHO as carcinogen class I for gastric cancer, but no association has been reported with colorectal neoplasia

AIMS & METHODS: The aim of this pilot study was to investigate the incidence of H. pylori infection in colonic tumour biopsy specimens and to evaluate the oncogenes' expression involved in colorectal carcinogenesis. 11 patients (10 male, 1 female, mean age 72.4±7.9 years) with colorectal cancer underwent low GI tract endoscopy. On colonoscopy were obtained biopsy specimens (n=6-8) from tumour and adjacent normal colonic tissue for evaluation of: (a) presence of H. pylori histologically with Cresyl Violet and/or Giemsa stains; (b) expression of oncogenes Ki67, p53, Bcl-2 and Bax by immunohistochemistry; (c) T- (CD45RO) and B- (CD20) lymphocyte infiltration of colonic mucosa by immunohistochemistry. Moreover, serum samples were collected for the assessment of serum gastrin by radioimmunoassay (RIA) (normal value <108 pg/ml).

RESULTS: Histologic presence of H. pylori infection was found in 10 out of 11 (90.9%) colonic biopsy specimens. Mean serum gastrin levels were found 70±14 pg/ml. Ki67 expression was increased (>50%) in all tumour specimens and low (<10%) in all adjacent normal tissue specimens. p53 expression was increased (>50%) in 8 out of 11 (72.7%) tumour specimens and low (<10%) in all adjacent tissue specimens. Bcl-2 expression was increased (60%) in one tumour specimen and low (<10%) in all adjacent tissue specimens. Bax expression was increased (50%) in one tumour specimen and low (<10%) in all adjacent tissue specimens. T-lymphocyte infiltration was mild in 6 (54.5%) and moderate in 5 (45.5%) out of 11 patients. Mild B-lymphocyte infiltration was found in 3 (27.3%) patients.

CONCLUSION: A high incidence of H. pylori infection colonising colonic tumour tissue was documented, thereby indicating a potential pathogenetic role of H. pylori on colorectal carcinogenesis. H. pylori colonisation was associated with an increased cell proliferation and impaired apoptotic process in tumour specimens compared with the normal adjacent colonic tissue. Serum gastrin levels seem to have no impact on colorectal carcinogenesis.

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HIGH DETECTION RATE OF CYTOMEGALOVIRUS (CMV) GENOME IN GASTRIC ADENOCARCINOMA AND PRECURSOR LESIONS TISSUE SAMPLES. A POSSIBLE ROLE IN THE PATHOGENESIS OF THE DISEASE?

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INTRODUCTION: Human carcinogenesis is a multifactorial process. The etiological factors and mechanisms still remain unclear. In many cases viruses and bacterias are involved. The aim of the present study was to estimate a possible role of CMV, alone or in correlation with helicobacter pylori (HP), in the pathogenesis of gastric adenocarcinoma.

AIMS & METHODS: A total of 80 non immunocompromised patients 40 with gastric cancer and 40 with premalignant lesions (chronic gastritis, gastric atrophy, intestinal metaplasia, gastric polyps) as well as 80 individuals with non endoscopic evident gastric disease, considered as control group, were enrolled in the study. Were obtained bioptic specimens from the malignant and the premalignant lesions, 3 cm away from the lesions and also from endoscopically healthy mucosa from the patients and the control group. The method used to identify the CMV genome was polymerase chain reaction (PCR). The presence of HP was investigated with CLO test and histological examination of mucosal gastric samples from the antrum and/or the corpus of the stomach. Multivariate statistical analysis was performed correlating the results with epidemiological parameters (age, sex, smoking, alcohol) which may be involved in the pathogenesis of the disease

RESULTS: The viral genome was detected in 11 out of 40 (27.5%) tissue samples from malignant lesions, in 15 out of 40 (37.5%) samples from premalignant lesions, but in none of the bioptic specimens from endoscopically healthy mucosa either from patients or from the control group. The X2 performed statistical analysis revealed a significant difference in the detection rate between the control population and the two examined groups of patients ($p<0.001$). No significant statistical correlation was observed between the detection rate of viral genome and the detection rate of HP in the two examined groups of patients ($p=0.999$ and $p=0.317$ respectively) and also between the detection rate of CMV and the epidemiological parameters involved in gastric carcinogenesis

CONCLUSION: Our results indicate a possible role of CMV in the gastric adenocarcinoma pathogenesis as an independent factor in a subgroup of patients.

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EVALUATION OF A NEW NEAR-PATIENT ANTIGEN STOOL TEST FOR THE DETECTION OF HELICOBACTER PYLORI

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INTRODUCTION: The detection of Helicobacter pylori (H. pylori) antigen in stool is a reliable non-invasive method for the diagnosis of H. pylori infection in untreated patients. Recently, in-office stool tests have been developed allowing the rapid detection of H. pylori antigen.

AIMS & METHODS: We compared a new near-patient immunochromatographic stool test (Simple H Pyl) with the standard enzyme-linked immunoassay (HpSA). Fifty H. Pylori positive and 50 negative patients who underwent esophago-gastro-duodenoscopy were selected over a period of 18 months. H. pylori infection was diagnosed by using histology (Giemsa stain), rapid urease test and urea breath test (UBT). Patients were classified as H. pylori positive if 2 of the 3 tests were positive and H. pylori negative if all the 3 tests were negative. Equivocal cases were excluded. Fresh stool samples were stored at -20° C until testing. We assessed the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), overall diagnostic accuracy (ODA) and cost of Simple H Pyl and HpSA and compared them with UBT.

RESULTS: The mean age of the patients was 55.8 years (range 23-80). The results are shown below (table). ROC curve analysis showed a cutoff value of 0.144 for HpSA. The cost was 24.2 Euros for HpSA, 23.8 for Simple H. Pyl and 55.7 for UBT

	Sensitivity	Specificity	PPV	NPV	ODA
HpSA	82%	94%	93%	92%	88%
Simple H. Pyl	78%	78%	76%	78%	79%
UBT	100%	100%	100%	100%	100%
Biopsy	100%	100%	100%	100%	100%
CLO test	94%	96%	96%	94%	95%

CONCLUSION: The overall performance of the Simple H pyl test is lower compared to UBT, HpSA and CLO test. HpSA is cheaper and should be preferred to UBT if available in the primary care setting.

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Molecular and Immunohistochemical Evaluation of the Expression of Telomerase in Gastric Carcinomas: Correlation with H. pylori Infection

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Telomerase is an enzyme associated with cellular immortaliazation and plays an important role in carcinogenesis. Telomerase adds hexameric repeats of 5'-TTAGGG-3' to the ends of chromosomal DNA called telomerase, the length of which increase proportionally to the cellular activation rate. Telomerase consists of 2 subunits, Telomerase RNA template (hTR) and Telomerase reverse transcriptase protein (hTERT).

Aim: To define hTR activity in the serum of H. pylori related gastric carcinoma patients and to compare these findings with the immunohistochemical expression of Telomerase in bioptic material taken from the same patients. Telomerase activity was measures by using the QIAGEN IneStep RT-PCR kit in human serum of 45 H. pylori-related gastric carcinoma cases (22 diffuse and 23 intestinal type). Histologically, Intestinal Metaplasia (IM) type I was observed in 5 cases, type II in 8and type III in 12 cases. The expression of Telomerase in the tissues was assessed immunohistochemically using a anti-Telomerase Moab (Novocastra, UK). Positive and negative controls were also included.

Results: Increased hTR activity as well as immunohistochemical expression of tissue Telomerase detected in 43/45 cases examined. In normal gastric mucosa, weak hTR expression was noted, limited to basal cells of gastric glands. hTR activity and Telomerase expression found to be higher in IM of type III than in type I and II (4:2:1 accordingly). H. pylori-negative controls constantly expressed very low levels of hTR activity.

Conclusion: H. pylori infection may be a strong trigger for hTR overecpression possibly through activation of epithelial "stem cells" during the procedure of intestinal metaplasia.