10. Ulcer diseases (including NSAIDs)

10.01 \textit{Helicobacter pylori} infection increases the risk of gastro-duodenal damage in elderly subjects taking low-dose aspirin

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\textbf{With the aim} to evaluate the effect of \textit{H. pylori} infection on the risk of low-dose aspirin-related upper GI lesions in the elderly we studied 189 symptomatic low dose aspirin chronic users (M=94,F=95, mean age=80.2 years, range 66-96) who underwent an endoscopy. A structured interview was carried out to evaluate the use of gastroprotective drugs (misoprostol or PPIs in active dosage for at least one month) and aspirin. Chronic low-dose aspirin user was defined as a patient who was continuously taking aspirin at the dosages of 75 mg to 300 mg daily at least during the last three months. \textit{H. pylori} infection was diagnosed by histology and the rapid urease test on 2 antral and 2 body gastric biopsies.

\textbf{Results:} According to the presence of \textit{H. pylori} infection, 97 patients were \textit{H. pylori} positive and 92 patients were \textit{H. pylori} negative. A significant higher prevalence of peptic ulcer (40.2\% vs 17.4\%, p=0.001) and bleeding lesions (6.2\% vs 0.8\%, p<0.05) were observed in \textit{H. pylori}-positive versus \textit{H. pylori}-negative subjects. \textit{H. pylori} infection increased the risk of peptic ulcer (OR=6.6, 95%CI=3.3-13.3) and bleeding lesions (OR=7.9, 95%CI=1.6-40), while the absence of \textit{H. pylori} infection decreased the risk of gastroduodenal damage (OR=0.14, 95%CI=0.07-0.30). The use of PPIs decreased the risk of peptic ulcer (OR=0.21, 95%CI=0.09-0.48) and bleeding (OR=0.29, 95%CI=0.03-2.52); the treatment with nitrovasodilators did not influence the risk of damage in this population.

\textbf{Conclusions:} In elderly chronic users of low-dose aspirin, \textit{H. pylori} infection significantly increased the risk of peptic ulcer and upper GI bleeding; in contrast, the co-treatment with PPIs reduced such a risk. To test (as well as to treat) \textit{H. pylori} infection may be a useful strategy to prevent gastroduodenal damage in elderly patients who need to take low-dose aspirin.

10.02 \textit{Helicobacter pylori} related gastric carcinogenesis and immunohistochemical expression of FHT gene product

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\textbf{Background:} Changes in the fragile carcinogenic region FRA3B of Frigilino histidine triad (Fhit) gene have been proposed as an early event in gastric carcinogenesis. We investigated the immunohistochemical expression of Fhit gene product (protein) in biopsies of patients diagnosed with chronic gastritis [\textit{Helicobacter pylori} (Hp) related or not], gastric epithelial dysplasia, intestinal metaplasia and gastric adenocarcinoma

\textbf{Materials and Methods:} We performed immunohistochemistry in archival material of formalin-fixed, paraffin-embedded tissues of 135 gastric biopsies (76 endoscopic and 59 surgical), using the anti-Fhit antibody (rabbit anti-Fhit polyclonal antibody, ZYMED) and the streptavidin-biotin peroxidase method ( Dakopatts). Biopsies from normal gastric epithelium were used as controls. Depending on the strength of staining for Fhit all biopsies were characterized as negative (0) up to strongly positive (3+) ones. Statistical analysis was performed with Fischer’s exact test and McNemar’s x² test.

\textbf{Results:} Total absence or minimal expression of Fhit protein was noticed in 79% of Hp positive(+) gastritis, in 76.4% of chronic gastritis with low or high grade dysplasia and in 56% of gastric adenocarcinomas. The absence of Fhit protein expression correlated with the presence of Hp (p=0.0001) and epithelial dysplasia (p=0.01) but not with enteric metaplasia. Moreover, a correlation was noticed between the absence of Fhit expression and the infiltrating phenotype of gastric adenocarcinoma (p=0.02) as well as with its histological and clinical staging (p=0.01).

\textbf{Conclusions:} Our results strongly indicate that absent or reduced expression of Fhit protein in Hp(+) gastritis or chronic gastritis with dysplasia, may be an early event in gastric carcinogenesis, probably through direct or indirect changes in the fragile region of the Fhit gene.

10.03 Risk of peptic ulceration related to \textit{H. infection}, non-steroidal anti-inflammatory drug (NSAID) and tobacco usage in dyspeptic population

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\textbf{Background:} Peptic ulceration is an important sociomedical problem causing life-threatening complications such as gastro-intestinal bleeding and ulcer perforations. \textit{H. pylori}, NSAID and cigarette smoking are major risk factors for gastro-duodenal ulcers. However, studies on interaction between these factors are controversial.

\textbf{Aims:} 1) to examine the association between gastro-duodenal ulcers and \textit{H. pylori} infection, NSAID use, age and smoking, 2) to assess the relationship between \textit{H. pylori}, NSAID and smoking, age and family history in development of ulcers among dyspeptic patients, 3) to identify idiopathic gastro-duodenal ulcers and their proportion to all ulcers detected in the study sample of dyspeptic patients.

\textbf{Subjects and Methods:} 5967 dyspeptic patients (mean age 52 ± 12 yr.) who underwent low-dose capsule\textsuperscript{17}C-urea breath test (UBT) and upper endoscopy, while their age, family link and dyspeptic symptoms were reported.

\textbf{Results:} Out of 5967 patients, 31.8% were ulcerated. 9.2% had gastric, 17.2% duodenal and 5.4% both gastric and duodenal ulcers. The \textit{H. pylori} was found in 64.8% dyspeptic patients and among 72.6%, 83.6% and 76.9% of gastric, duodenal and gastro-duodenal ulcers. Ulceration was related to \textit{H. pylori} significantly and ORs were: 1.44 and 1.81, respectively. NSAID was used by 6.2-12.7% of ulcer patients and the ulcer risk rose only in GU group. The \textit{H. pylori} prevalence was higher in smokers (76%) than in non-smokers (67%). About 19% of ulcers were “idiopathic” i.e. without NSAID and \textit{H. pylori}. 57% of all patients reported a family history of peptic ulcers.

\textbf{Conclusions:} 1) The results of multivariable logistic regression model confirms that aging, \textit{H. pylori} infection, NSAID use and smoking play significant role in peptic ulceration; 2) There is an evidence for negative interaction, suggesting that \textit{H. pylori} may prevent the development of ulcers in NSAID users; 3) About 19% of ulcers are idiopathic and age dependent.

10.04 Antagonistic and synergistic interaction between \textit{Helicobacter pylori} (Hp) and conventional nonsteroidal anti-inflammatory drugs (NSAID) and Coxibs during healing of preexisting gastric ulcers

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\textbf{Background:} Hp and NSAID such as aspirin (ASA) are independent risk factors of gastric ulcergenesis but interaction between them remains unclear.

\textbf{Aim:} to compare the ulcer healing effects of gastric inoculation with viable Hp and its water extracts (WE) with those of vehicle in animals with or without concurrent intragastric (i.g.) administration of acetylsalicylic ASA (50 mg/kg/d) and rofecoxib (10 mg/kg/d) that started one week upon Hp and Hp-WE (series A) or prior to Hp, Hp-WE or saline inoculation (series B).

\textbf{Methods:} Gastric ulcers (GU) were induced in rats by acetic acid. Animals were killed (day 12 and 20) upon Hp inoculation and ulcer induction. GU area, gastric blood flow (GBF), gastric mucus secretion and...
mRNA expression for IL-1beta and TNFalpha as well as gastrin, IL-1beta, and TNFalpha plasma concentrations were determined.

**Results:** GU healed and reduced area by 59% and 97% in controls at day 12 and 20. Inoculation with Hp and Hp-WE or ASA and rofecoxib, each applied alone, delayed ulcer healing and decreased GBF but increased 2-3 fold IL-1beta and TNFalpha mRNA. In Hp-infected rats ASA or rofecoxib attenuated area of GU, plasma IL-1beta and TNFalpha levels but increased GBF comparing to ASA or rofecoxib applied alone. In contrast, ASA or rofecoxib, administered before inoculation with Hp and Hp-WE, increased the ulcer area, IL-1beta and TNFalpha concentrations but reduced GBF significantly.

**Conclusions:** 1) GBF impairment in the ulcer area, over-expression and release of IL-1beta and TNFalpha may prolong ulcer healing induced by Hp and Hp-WE. 2) Hp induced gastric inflammation may limit ASA deleterious effect and suggest “protective” action of preexisting Hp infection, 3) delayed healing in rats treated with ASA and then exposed to Hp and Hp-WE could be due to the failure in gastric adaptation to these NSAID-infected gastric mucosa.

### 10.05 Inflammation and intestinal metaplasia of cardiac mucosa in patients with duodenal ulcer disease and reflux esophagitis

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**Aim of the study:** To evaluate possible differences in inflammation and intestinal metaplasia in patients with duodenal ulcer (DU) and reflux esophagitis (RE)

**Patients and Methods:** 90 patients with DU, all Hp(+) and 98 patients with RE, 54 Hp(+) and 44 Hp(-) were enrolled in the study. Biopsy specimens obtained from gastric antrum (A), fundus (F) and cardia(C) were examined with Hematoxylin-Eosin, modified Giemsa, PAS-Alcian Blue and H&E-Alcian Blue stains. The grade and activity of inflammation were evaluated according to updated Sydney System. Serology for CagA characterization was performed in all Hp(-) patients. Stat: chi-square.

**Results:** The number of patients with the different degrees (0/1/2/3) of the grade and the activity of inflammation as well as the presence and the extent of intestinal metaplasia (IM) are shown in the table. CagA seropositivity was 90% for DU patients but only 40% for REHp(+).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Activity</th>
<th>IM</th>
</tr>
</thead>
<tbody>
<tr>
<td>DU</td>
<td>0/16/40/34</td>
<td>4/14/22/40</td>
</tr>
<tr>
<td>p</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>REHp(+)</td>
<td>2/12/34/60</td>
<td>7/17/24/60</td>
</tr>
<tr>
<td>p</td>
<td>**</td>
<td>**</td>
</tr>
<tr>
<td>REHp(-)</td>
<td>2/28/14/40</td>
<td>34/8/22/0</td>
</tr>
</tbody>
</table>

*p<0.001, **p<0.0001.

**Conclusions:** 1) The grade and activity of the inflammation of the cardia are more severe in DU than in REHp(+) patients. 2) The grade and activity of the cardia inflammation are more severe in REHp(+) than in REHp(-) patients. 3) There is no difference in the presence of IM neither between DU and REHp(+) nor between REHp(+) and REHp(-) patients. 4) the prevalence of CagA seropositivity is higher in DU than in REHp(+) patients.

### 10.06 Augmentative effect of the gastric mucosal lesion on Helicobacter pylori and stress

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We hypothesized that if H. pylori infection or stress can induce oxidative damage in the stomach, the antioxidant can modulate the pathogenic course. We infected the SD rats or Mongolian gerbils with SS1 strain of H. pylori (VacA+, CagA+) and impose the water immersion restraint stress (WIRS) on experimental animals. WIRS was imposed for 30, 120 and 480 min, respectively in each group and sacrificed animals for gross and microscopic lesion scores, measurement of MDA, iNOS, GSH, transcription factors (NF-kB and AP-1), and RPA (cytokines and chemokines) from homogenate gastric mucosa, respectively. Significantly elevated levels of MDA, iNOS and decreased levels of GSH were observed in WIRS and H. pylori infected group compared to WIRS or H. pylori infection alone group. All stress and H. pylori infection at high risk of gastric cancer.

### 10.07 Evaluation of pepsinogen I in rheumatological patients regarding to H. pylori status, use of NSAIDs and gastroduodenal ulcers

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**Objective:** To investigate the value of pepsinogen I (PGI) as a screening tool for gastroduodenal damage in rheumatological patients.

**Aims:** To analyse serum levels of PGI in Helicobacter pylori (Hp) status, usage of NSAIDs and level of gastroduodenal lesions.

**Methods:** Gastroduodenal mucosa was evaluated during upper gastrointestinal endoscopy using Lanza score. The prevalence of Hp infection was evaluated by urease test and histology (modified Giemsa). Serum levels of PGI were measured using PGI-ELISA (Biohit, Finland). Statistic analyses were performed using T-test and ANOVA.

**Results:** 128 patients (78.1% women, mean age 57.2±13.1 years; 85.9% Hp-positive) were analyzed in context to NSAID usage. 25.8% patients did not use NSAIDs during the last week; 45.3% used nonselective NSAIDs, and 28.9% used selective Cox-2 inhibitors for at least one month. The mean value of serum PGI in Hp negative patients (51 U/ml±31) was lower than in Hp positive group (123 U/ml±100), p=0.003. PGI values were higher in patients having gastroduodenal ulcer (199 U/ml±168; p=0.001) compared to patients having normal mucosa (106 U/ml±95) or gastroduodenal erosions (95 U/ml±50).

There were no significant differences of PGI serum levels among patients with respect to the usage of NSAIDs. Patients without NSAIDs, with unselective NSAIDs and with selective Cox-2 inhibitors revealed similar PGI values of 102 U/ml±54, 124 U/ml±112, and 105 U/ml±101, respectively.

**Conclusions:** Serum PGI levels were higher in Hp positive patients compared to that of Hp negative. Serum levels of PGI were higher in patients with gastroduodenal ulcers compared to those without ulcers. No significant differences were found between PGI levels and the usage of NSAIDs. Due to wide ranges of PGI in the three groups evaluated, PGI is not of clinical value for gastroduodenal mucosa damage evaluation, neither concerning Hp status nor the usage of NSAIDs as predisposing factors.

### 10.08 Association of gastric metaplasia with Helicobacter positive peptic ulcers

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**Background:** Gastric metaplasia (GM) is the basis of an Hp-infection in the duodenal bulb. Because GM can be found also in asymptomatic subjects, it has been suggested to be a normal finding.

**Objective:** To study the presence of GM in Helicobacter infected peptic ulcer and chronic gastritis (CG) patients and in Helicobacter negative non-ulcer patients (Non-ulcer).

**Methods and subjects:** 392 patients with upper abdominal symptoms were endoscoped (ulcer patients also 8 weeks later) for medical indications. ASA- and NSAID-users were not excluded. Duodenal ulcers (DU), prepyloric ulcers (PPU) and typical gastric ulcers near angulus in the lesser curvature (GU) were recorded separately. Hp infection was detected by a positive result in culture, histology (according to the Sydney system with GM grading 0-3) of the biopsies or serology by our in-house EIA-test.

**Results:** Moderate and strong GM were most common in patients with DU (p < 0.001) in comparison with patients of each other diagnostic group.
nositic group. Patients with PPU also differed from the Non-ulcer- and CG-groups (p = 0.0142 and 0.0241 respectively), but no other significant differences between the groups were found. The risk of peptic ulceration associated with moderate and strong GM decreased in the order presented in the table.

Number of patients with different gastric metaplasia scores in different diagnostic groups.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>GM 0-1</th>
<th>GM 2-3</th>
<th>% GM 2-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>DU</td>
<td>17</td>
<td>43</td>
<td>72</td>
</tr>
<tr>
<td>PPU</td>
<td>19</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>GU</td>
<td>13</td>
<td>27</td>
<td>13</td>
</tr>
<tr>
<td>CG</td>
<td>140</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Non-ulcer</td>
<td>132</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>321</td>
<td>71</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: GM was found to be an important risk factor of peptic ulceration. Significantly higher prevalence rates of moderate and strong GM scores in H. pylori-infected patients with DU and PPU in comparison with other diagnostic groups studied indicate that the grade of GM may influence the localisation of a peptic ulcer.

10.09 Meta-analysis of the effect of *H. pylori* eradication therapy on the prevention of recurrent ulcer bleeding


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Purpose: To evaluate whether *H. pylori* eradication therapy is more effective than long-term maintenance antisecretory therapy in the prevention of recurrent haemorrhage from peptic ulcer.


Study selection: Trials which compared the effect of eradication therapy versus maintenance antisecretory treatment on the recurrence of ulcer bleeding were included. Studies with all patients taking NSAIDs or less than 6 months of follow-up were excluded. Data extraction: Meta-analysis combining the Odds Ratios (OR) of the individual studies in a global OR (Peto method) was performed, and number needed to treat (NNT) was calculated.

Results: Ten studies fulfilled the inclusion criteria. Recurrent bleeding was reported in 2.2% (95%CI=1.2-4%) of the patients who received eradication treatment and in 10.5% (7.5-13%) of those treated with antisecretory therapy (OR=0.19; 0.11-0.34). NNT with eradication therapy (compared with antisecretory therapy) to prevent one relapsing episode was 12. When patients taking NSAIDs were excluded, recurrent haemorrhage was observed in 2% (1-4.4%) of patients on eradication therapy and in 11% (7.2-14.8%) of those on long-term antisecretory treatment.

Conclusions: *H. pylori* eradication therapy is more effective than maintenance antisecretory treatment to prevent recurrence of peptic ulcer bleeding and, therefore, it must be considered in all such patients.

10.10 *Helicobacter pylori* infection and perforated peptic ulcer. Prevalence of the infection and role of antimicrobial treatment


La Princesa University Hospital, Madrid, Spain

Aim: To systematically review studies assessing the prevalence of *H. pylori* (Hp) infection in patients with perforated peptic ulcer (PPU), the role of Hp in the recurrence of the ulcer perforation, and the effect of eradication on the recurrence of this complication.

Methods: Bibliographical searches were performed in PubMed database and abstracts from congresses until March 2002. Weighted mean of Hp prevalence was calculated. The effect of Hp infection and Hp eradication on the recurrence of the ulcer or the ulcer perforation was assessed.

Results: Nineteen studies were found, including 1,169 patients. Mean Hp prevalence in PPU was 68.1% (95%CI=65-71%). Some case-control studies found a lack of association of PPU and Hp, while others found no significant differences between Hp prevalence in PPU and in non-perforated peptic ulcer. These controversial results may be due to differences in: a) NSAID use (which in some studies was associated with Hp-negative PPU); b) ulcer location (mean Hp infection rate in studies including only duodenal ulcers was even lower (61%) than in those including only gastric ulcers (72%)); c) sensitivity of diagnostic methods (when 3 or more methods were used, Hp prevalence increased to almost 100%); and d) previous Hp eradication by procedures aimed to treat PPU (antibiotics, vagotomy or gastrectomy). In several studies, recurrent ulcer after PPU mainly occurred in infected patients. Other studies demonstrated that most patients remained ulcer-free and perforation-free after Hp eradication.

Conclusion: Mean Hp prevalence in PPU is of only 65-70%. However, infection rates ranged from 6% to 100%, suggesting that differences in variables as number or type of diagnostic methods, or NSAID use, may be responsible for the low prevalence in some studies. PPU should be treated by simple closure and with Hp eradication, as it prevents recurrence of the ulcer and the ulcer perforation.

10.11 *Helicobacter pylori* infection and gastric outlet obstruction. Prevalence of the infection and role of antimicrobial treatment


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Aim: To systematically review studies assessing *H. pylori* (Hp) prevalence in patients with gastric outlet obstruction (GOO), and to evaluate the effect of *H. pylori* eradication on the resolution of this complication.

Methods: Bibliographical searches in Internet until March 2002. Key words: pylori and (obstruction or stenosis or “gastric outlet obstruction”). Weighted mean of prevalence and 95% confidence interval (95%CI) was calculated. The effect of *H. pylori* eradication on the resolution of GOO was assessed in all studies.

Results: From 7 studies, including 187 patients with GOO, an overall Hp prevalence of 69% was calculated (95%CI=62-76%). However, Hp infection rates in various studies ranged from 33% to 91%, suggesting that differences in variables as number and type of diagnostic methods, or frequency of NSAID use, may be responsible for the low prevalence reported in some studies. The only case-control study directly comparing ulcer patients with and without GOO demonstrated similar Hp infection rates (91% vs. 95%). Resolution of GOO after eradication of Hp has been demonstrated in 9 studies. It seems that the beneficial effect of Hp eradication on GOO is observed early, just a few weeks after antimicrobial treatment. Furthermore, this favorable effect seems to remain in the long-term follow-up. Nevertheless, GOO does not always resolve after Hp eradication treatment and the explanation for the failures is not completely known. NSAID intake perhaps plays a major role in these cases. Some studies suggest that treatment should start pharmacologically with the eradication of Hp even when the stenosis is considered to be fibrotic or when there is some gastric stasis.

Conclusion: Hp eradication therapy should be considered the first step in the treatment of duodenal or pyloric Hp-positive stenosis, whereas dilation or surgery should be reserved for patients who do not respond to such medical therapy.

10.12 A study on the efficacy of three-day versus seven-day rabeprazole-based triple therapy in the eradication of *Helicobacter pylori* in peptic ulcers

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Background and Objective Current standard for *Helicobacter pylori* eradication requires at least seven-days of therapy. Rabeprazole, new generation proton pump inhibitor has been shown to rapidly and strongly inhibit gastric acid secretion leading to earlier stabilization of antibiotics like clarithromycin. It is thus possible that the seven-day regimen could be further shortened. The objective of this study is to determine the efficacy of a three-day regimen versus a seven-day regimen of rabeprazole in combination with standard doses of clarithromycin and amoxicillin in the eradication of *H. pylori* infection in patients with documented active peptic ulcer disease.

Patients and Methods. This clinical trial is a single-center, randomized, open-label parallel group study on 113 Taiwanese subjects with documented *H. pylori* infection and active peptic ulcer disease. The trial comprised a treatment period of 3 or 7 days’ eradication regimen which consists of rabeprazole 20 mg bid plus clarithromycin 500 mg and amoxicillin 1 gram bid, rabeprazole 20 mg qd was continued up to the end of the 8th week. The *H. pylori* status was assessed by means of histology, rapid urease test and polymerase chain reaction (PCR) test for the detection of *H. pylori* DNA.

Results 113 patients were randomized (see table). Per protocol and intention-to-treat eradication rate were no significantly in the 7-day RAC.
Evolution of endoscopic incidence of
gastrroduodenal ulcer (GDU) and esophagitis (E)
after the wide application of Helicobacter pylori (Hp)
eradication regimens

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There are several recent reports suggesting a decrease in the incidence of GDU. The aim of our study was to evaluate if there are changes in the prevalence of endoscopic diagnosis of GDU or E after the wide application of Hp eradication regimens.

Patients & Methods: We analyzed all the endoscopic reports and related findings to patients who had an UGD endoscopy during the years 1993, 1997 and 2001. Our department is situated in a central hospital of Athens, it belongs to the National Health System (NHS) and has an open access for all beneficiaries of NHS.

Results: Total number of fiberoscopies (UGI), gastric/duodenal ulcers (GDU) and E with the corresponding LA classification (A/B/C/D) are shown on the table. The groups were comparable for age, tobacco and alcohol consumption. Valuable information on Hp status in patients with endoscopic lesions were available in only 58% during 1993, while this increased dramatically during 1997 (96%) and 2001 (97%). Among them, the % of Hp (+) patients was 50%, 42% and 51% for E, 77%, 65% and 73% for GU and 90%, 89% and 85% for DU for the 3 periods respectively. NSAID’s consumption was not modified according to the files data. Complications decreased only in 2001 (205, 196, 68).

Conclusions: Since 1993, 1) The total number of UGI procedures has not changed, 2) The accurate control on Hp status has dramatically increased, 3) Neither the prevalence of GDU and E at endoscopy nor their Hp status were modified, 4) Non variceal hemorrhage decreased during 2001, regardless of the same NSAID’s consumption.

Role of nitric oxide and prostaglandins in histamine-induced lesions in devascularized rat stomachs

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We recently established a new method to induce gastric lesions by administering histamine to rats with partially devascularized stomach and ligated-pylorus. This study examined the pathogenic mechanism of gastric lesion formation in this procedure.

Methods: Male Wistar rats were used after fasting. Under ether anesthesia, the gastric artery and the accompanying venous were ligated for partial devascularization of the stomach. The pylorus was ligated concurrently. Ten minutes later, histamine 2HCl (40 mg/kg) was administered sc twice (every 2 hours); the animals were killed 4 hours later. Gastric contents were analyzed for acid output, and the damaged area was determined under a dissecting microscope.

Results: Histamine significantly increased gastric acid secretion in normal rats with pylorus ligation alone. In contrast, similar treatment with histamine to rats with devascularized stomachs and ligated-pylorus did not stimulate gastric acid secretion compared with the control group. Nonetheless, severe mucosal damages were observed in the oxyntic area in the anterior and posterior walls in all animals. Histamine H2 receptor antagonists, given po 1h before pylorus ligation, significantly inhibited the lesion formation in a dose-related manner. The lesion formation was inhibited despite the absence of suppression of acid secretion. Histamine H1 receptor antagonists significantly inhibited the development of lesions. Gastric acid secretion was significantly increased in the H1 blocker treated-group. Such results suggest that gastric acid is not involved in the mechanism for the development of these lesions. NOS inhibitor significantly inhibited the development of lesions, while iNOS inhibitor (aminoguanidine, sc) had no effect on lesion formation. The development of lesions was also inhibited by pretreatment with indomethacin (sc).

Conclusion: The mechanism by which histamine induces gastric lesions in the above model appears to involve the ischemia-reperfusion system in the oxyntic mucosa mediated by means of NO and PGs.

A five year follow-up study after treatment of H. pylori in patients with peptic ulcer disease

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 Aim: To evaluate the recurrence rate of PUD after successful and unsuccessful H. pylori treatment.

Material and Methods: All of 107 (M 66, F 41, mean age 48 years) patients with duodenal ulcer (n=77) and gastric ulcer (n=30) were divided into two groups after H. pylori treatment: HPnegative group – 73 patients and HPpositive group – 34 patients. Ulcer healing was achieved in all patients after treatment and HP eradication was confirmed by three tests: histology, cytology, urease test on 5 antral and corpus biopsies. Repeat endoscopy with biopsy for urease test, histological and cytological examinations was performed at least annually in all of patients and as soon as possible when ulcer symptoms recurred during follow-up period. Smoking, alcohol and NSAIDs consumption, dietary changes were evaluated in all cases.

Results: Recurrent ulcers were detected in 15 (20%) patients from HPnegative group and in 28 (82.3%) patients (p<0.05) from HPpositive group. Remission rate was low – 2% per patient per year. The results of the study are shown in the table.

Conclusion: Ulcer recurrences are closely related to presence of H. pylori infection and may be related to usage of NSAIDs and smoking. H. pylori eradication reduces the recurrence rate of PUD.

Investigation of coccoid Helicobacter pylori forms in ulcer disease relapses by means of PCR

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Ulcer Disease relapation after antimicrobial therapy can not always be explained by H. pylori-resistance to antibiotics. It is known that under unfavorable conditions of environment H. pylori can transform into non-active coccoid forms. These forms do not display urease activity and it is rather difficult to diagnose them histologically. It leads to misappositive evaluation of antimicrobial treatment effectiveness.

35 patients with ulcer disease were investigated. All patients undergo EGDS with aimed biopsy of gastroduodenal mucous before and after 4 weeks after antimicrobial treatment. Bioplates were investigated by means of fast urease test, histologically and PCR on H. pylori. Repeated investigation was carried out 6 months afterwards treatment.

After antimicrobial treatment 25 patients had negative results on H. pylori according to urease as well as histological and PCR methods of
Absence of Helicobacter pylori infection in patients with duodenal peptic ulcer

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Background: The role of Helicobacter pylori (Hp) infection in peptic ulcer had been elucidated in the last decade. Recently, it has been reported that there have been an increase in Hp(-) peptic ulcer disease. We aimed to determine the prevalence of the absence of Hp infection in patients with duodenal lesions (duodenal ulcer, erythematous duodenitis, erosive duodenitis).

Methods: Patients with duodenal lesions out of 737 endoscopic examinations between 10/2000-4/2002 included in the study. Diagnostic methods for determining Hp infection were endoscopic biopsy (two samples from antrum and body for rapid urease test), histological study (two samples from antrum and body for haematoxylin and eosin staining) and qualitative Hp IgG testing.

Results: There have been 144 duodenal ulcer, 76 erythematous duodenitis and 47 erosive duodenitis cases in 737 patients. Hp infection was absent in 38.2% of patients with duodenal ulcer, in 61.9% of erythematous duodenitis and in 42.6% of erosive duodenitis.

Conclusion: Hp(-) duodenal lesions are more than presumed. Increase in the absence of Hp infection in patients with duodenal lesions may be a result of widespread empiric anti-Hp therapies.

Smoking is associated with increased risk for duodenal ulcer in Helicobacter pylori-infected patients in Taiwan

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Background and Aims: Although Helicobacter pylori has been established as a major etiologic factor of chronic gastritis and makes an important contribution to peptic ulceration, the reason why H. pylori causes different gastroduodenal disease in different people is not clear. The aim of this study was to identify risk factors associated with duodenal ulcer in H. pylori-infected patients in a multivariate context.

Methods: Demographic data, personal habits, NSAID use, stressful life events in previous 6 months, psychological distress, serum pepsinogen I and cortisol concentrations were studied in 70 consecutive dyspeptic patients with duodenal ulcer and 40 patients with functional dyspepsia.

Results: Compared to patients with functional dyspepsia, patients with duodenal ulcer had more ulcer-like dyspepsia but less dysmotility and reflux-like dyspepsia defined by symptom clusters. Patients with functional dyspepsia had more somatic complaints than those with duodenal ulcer. Univariate analysis showed that proportion of male gender (p=0.002) and smoking (p<0.001), and serum pepsinogen I levels (p=0.001) are higher in patients with duodenal ulcer than those with functional dyspepsia. On the other hand, serum cortisol levels are higher in patients with functional dyspepsia as compared to patients with duodenal ulcer (p=0.076). There was no significant difference in the stressful life events and psychological distress between the two groups. Multivariate analysis shows that smoker (odds ratio=5.7, 95% CI=1.7-19.0, p=0.0051) was associated with duodenal ulcer disease.

Conclusion: This study suggests that smoking is a major risk for occurrence of duodenal ulcer in H. pylori-infected patients in Taiwan.
Results: Eradication rate: intention-to-treat - group 1: 79.3% (64.6-94.0%; 95% IC) versus group 2: 75.9% (60.4-91.4%; 95%IC) NS; per protocol analysis - group 1 82.5% (66.9-96.1%; 95%IC) versus group 2: 81.5% (66.9-96.1%; 95%IC) NS.

Side effects were infrequent and mild.

Conclusion: this study showed that a one week Proton Pump Inhibitor-Based Triple Therapy is well tolerated and has similar efficacy as an identical two weeks regimen for Helicobacter pylori eradication.

10.23 Bleeding peptic ulcer in Japan: Role of Helicobacter pylori infection and NSAIDs use


Aim: The aim of this study is to investigate the characteristics of bleeding peptic ulcer in Japan, including the role of H. pylori infection and NSAIDs use.

Patients and Methods: This study was prospectively intended for patients who have a bleeding peptic ulcer at emergent endoscopy in our hospital in 1998 to 2001. We grouped these patients by H. pylori infection and NSAIDs use, and examined backgrounds of patients; i.e., age, sex, underlying disease, location of ulcer.

Results: We divided 128 patients with bleeding gastric or duodenal ulcer into 4 groups. Group A (71, 55.5%); H. pylori (+), NSAIDs (-), Group B (10, 7.8%); H. pylori (+), NSAIDs (+). Group C (14, 10.9%); H. pylori (-), NSAIDs (+). Group D (33, 25.8%); H. pylori (-), NSAIDs (-). Age in patients with use of NSAIDs was high (Group B and C). Age Group C, females were more than males. Corporeal ulcer of group D was higher than that of group A. Duodenal ulcer of group A was higher than that in other groups. Most of patients with Group B, C, had underlying disease compared to patients with H. pylori related ulcer (Group A). But, the underlying disease of Group D was more severe than that of Group B and C. Contents of underlying diseases were liver cirrhosis, congestive heart failure, and coronary disease. Rebleeding cases were 5 of all, and each case was gastric ulcer. Death cases were 5 of all the patients, and the causes of the death were due to severe underlying diseases.

Conclusions: In Japan, The patients who have bleeding peptic ulcer without H. pylori infection and NSAIDs use were relatively high compared to that with H. pylori infection. And one of the characteristics in these patients was to have severe underlying disease.

10.24 Clinico-laboratorial and ultrastructural evaluation of modern antihelicobacterial complexes in peptic ulcer patients treatment

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Helicobacter pylori (HP) - eradication at peptic ulcer (PU) is of great meaning, because HP increases the relapses frequency, the danger of the illness. Threefold therapy consisting of Rabeprazole-R (Pariet), Clarithromycin-C (Klacid), Amoxicillin-A (Flemoxin-Solutab) possesses high antihelicobacterial activity.

Aims: to investigate the efficiency of application of R+C+A for curing PU patients, the influence of these drugs’ combination on ulcer healing, ultrastructure of gastric mucosa (GM), relationships of aggressiveness (AF) and defense factors (DF) in gastric juice, HP eradication.

38 duodenal PU patients were investigated. Healing of ulcer with soft scar was observed in two weeks in 61 (73.5%), in four weeks - 83 (100%) patients. After treatment the HP-eradication was observed in 79 (95.2%) patient, average round-the-clock pH stomach body increased from 1.5±0.4 to 4.9±0.5.

AF - the relationship between the proteolytic activity and the total pepsin concentration was decreased. Before treatment AF was 0.91±0.08, after treatment - 0.42±0.05; normal 0.3±0.04. After treatment gastric juice DF - relationship between the mucous protein concentration and proteolytic activity increased. DF before treatment 0.81±0.04; after treatment - 2.51±0.07; normal 2.87±0.00.

Parietal cells of the GM were found in the state of high functional activity before curing. Mucous granules of the cover epitheliocytes were often subjected to degeneration and formed the whole secretory fields. After treatment an active regeneration of the cover cells of epithelium was observed in the GM. Parietal cells were found to be in the state of functional rest. Mucous producing cells were in active state and contained many secretory granules to the apical parts. Chief, muc cells in the state of the mild activity. There were many small interepithelium lymphocytes in GM, which evidenced its active proliferation. Great number of endocrine somatostatin producing D-cells was found in the GM.

Comprehensive treatment R+C+A is quite an effective method for curing PU.

10.25 Helicobacter pylori and metabolic processes in mucous barrier of gastroduodenal zone in peptic ulcer patients in dynamic of the treatment

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The aim is to study the effectiveness of antihelicobacter complexes (AHC) in HP-positive peptic ulcer (PU) patients, as well as their influence on the state of metabolic processes at gastroduodenal zone barrier mucous (GZBM).

52 HP-positive PU patients were prescribed AHC: Rabeprazole (Pariet) + Clarithromycin (Klacid) + Amoxicillin (Flemoxin-Solutab), 24 HP-negative PU patients - Rabeprazole + Sucralfat.

All the PU patients had their clinical remission in 3-5 days, endoscopic remission in 28 days. HP-eradication has been achieved in 49(94.2%) of the HP-positive patients.

The PU being acute in HP-positive and HP-negative patients, it is characterized by the increase of the sialoproteins degradation to 1.9 and 1.5 times and the evident decrease of the fucoproteins production of the gastroduodenal mucosa (GM) to 2.6 and 1.8 times accordingly compared to normal. The back correllative connection has been established between mucoid production and the speed of its reneweness (r = -0.74).

As result of the HP-positive and HP-negative patients treatment the level of N-acetylmuramic acid has been decreased to 1.4 and 1.6 times, the production of GM fucoproteins has increased to 2.4 and 1.6 times, it being compared with the data before treatment.

Mucous granules of the cover epitheliocytes of the GM were often subjected to degeneration and formed the whole sector fields, they making the outlet of the GM into the lumen of the stomach. After treatment the mucous producing cells were in active state, contained many secretory granules to the apical parts. There were many small interepithelium lymphocytes in GM which evidenced their active proliferation.

At the stage of clinico-endoscopic PU remission the complete normalization of the protective function at GZBM hasn’t been noticed and metabolic disturbances have been present, they increasing could lead to recidivation of the disease.

Conclusion: The most evident metabolic and ultrastructure changes, proving the weakening of the GZBM resistance have been found in HP-positive PU patients.