Helicobacter

European Helicobacter Study Group

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Accepted Abstracts

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Workshop Presentations

Workshop 1 Microbiology

Abstract no.: W1.1

METHYLOME DYNAMICS IN *H. PYLORI*

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Epigenetic DNA methylation affects gene expression and genome maintenance. *Helicobacter pylori* have many sequence-specific DNA methyltransferase genes, with different strains having unique repertoires. With a Pac Bio machine, we detected N6-methyladenines and N4-methylcytosines throughout the genome for five strains. The methylome was variable among closely related strains. Hypermethylated regions were found in *rpoB* gene for RNA polymerase and others. We identified DNA sequence motifs for methylation and then assigned each to a specific homology group of the target recognition domains in the specificity-determining genes. The results demonstrated that they often change DNA sequence specificity through domain movement_the movement between and within genes of coding sequences of target recognition domains. Knocking out one of the Type I specificity genes led to transcriptome changes, which suggested its role in gene expression. These results are consistent with the concept of evolution driven by epigenetic DNA methylation, in which various changes in the methylome lead to changes in the transcriptome and potentially to changes in phenotype (Furuta, Namba-Fukuyo, Shibata, Nishiyama, Shigenobu, Suzuki, Sugano, Hasebe, Kobayashi. PLoS Genetics, 2014).

A DNA methyltransferase is often paired with a restriction enzyme to form a restriction-modification system. Based on gene mobility, we identified a superfamily (PabI) of restriction enzymes with a novel fold (Half Pipe) in *H. pylori* and others. One of them excises a base from its recognition sequence (Miyazono, Furuta, Watanabe-Matsui, Miyakawa, Ito, Kobayashi, Tanokura. Nature Communications, 2014). This finding links epigenetic DNA methylation in prokaryotes and eukaryotes.

Abstract no.: W1.2

WHERE DID THE *HELICOBACTER PYLORI* PROPHAGES CAME FROM?

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Prophages are bacteriophage genomes that are inserted within the host bacterial genome and are stably replicated within that bacterial genome. We aimed to understand the exact time at which prophage genomes were integrated into the genome of *Helicobacter pylori*, a bacterium known to accompany humans in great migration events. Our study consisted of collecting 875 *H. pylori* DNA samples which were screened for the presence of two bacteriophage genes, integrase and holin. Less than 10% of the strains present both genes. PCR products were sequenced and the assembled sequences were concatenated and used to construct phylogenetic trees. Up until now we have selected 24 positive strains for both integrase and holin genes that were typed by MultiLocus Sequence Typing (MLST). The seven concatenated housekeeping gene sequences were analyzed phylogenetically (Neighbor-Joining method), together with those of 90 strains from 9 previously described *H. pylori* populations (PubMLST.org). The analysis of the phylogenetic trees (MLST & prophages) suggests that nearly 2/3 of the prophage positive strains present similar clustering to that of the MLST tree, while 1/3 have distinctive positions. However, this latter group tends to cluster with strains from the same geographic origin. These results suggest that about 2/3 of the prophage genomes were present in the *H. pylori* genome before *H. pylori* went out of Africa and that nearly 1/3 of the prophages were acquired later, in specific niches in the same geographic localization. Prophages are an additional player in *H. pylori* genome plasticity. Supported by grants UM.C/HIR/MOHE/13/5 (h-50001-00-A000033) and FCT-project PTDC/EBB-EBI/119860/2010.

Abstract no.: W1.3

COMPARATIVE GENOME ANALYSIS OF TWO *HELICOBACTER PYLORI* STRAINS ISOLATED FROM THE SAME PATIENT

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Two *Helicobacter pylori* (HP) strains (391-A/s and 391-A/l) were isolated from gastric mucosa of HP-seropositive patient with chronic gastritis under systemic lupus erythematosus. Strain 391-A/l was isolated from antral as well as from corpus mucosa and strain 391-A/s from antral mucosa only. Both strains were isolated using conventional methods and identified by MALDI-TOF and PCR techniques. 391-A/s and 391-A/l strains differ by the morphology and size of their colonies, urease activity and triphenyl-tetrazolium chloride reducing capacity. In order to reveal genetic differences between these two strains, we determined their draft genome sequences by parallel pyrosequencing approach. Nucleotide sequences of the genomes of 391-A/s and 391-A/l strains are highly similar to each other but both genomes have less than 96% homology to any other known complete HP genomes. Pairwise comparison of genome sequences of strains 391-A/s and 391-A/l reveals 1556 point polymorphisms in 216 protein-coding genes. Notably, nucleotide sequences of ureAB genes of urease operon and accessory genes ureIEFGD are completely identical in both strains. The difference in urease activity may be related to nickel transport and incorporation systems, as suggested by the polymorphism in nickel responsive regulator gene nikR, known to mediate regulation of metal metabolism and urease expression. Genomic differences between two strains are also found in genes coding for flagellar biosynthesis proteins, several outer membrane proteins, [NiFe] hydrogenase assembly protein HypC, and some enzymes of central metabolic pathways. Both strains lack cag-PAI pathogenicity island and contain similar but non-identical circular plasmids about 5 kb long.

Abstract no.: W1.4

MIR-155 EXPRESSION IN *HELICOBACTER PYLORI* INFECTED GASTRIC MUCOSA

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Introduction: *H. pylori*-triggered inflammation is a dynamic process that induces the cascade of gastric carcinogenesis. Understanding of this process in detail is crucial for the development of prevention strategies, in particular once irreversible alterations, such as intestinal metaplasia, have occurred. Recently, microRNA (miRNA) miR-155 has been linked with H.pylori-associated inflammation, but systematic analyses are not available yet. Here, we extensively analyzed miR-155 expression in gastric mucosa with regard to H.pylori infection/genotype and inflammatory/precancerous condition.

Methods: In the prospective study (HELDIVPAT/ERANET), 217 patients (normal mucosa (N), chronic gastritis (CG), atrophic gastritis +/- intestinal metaplasia (AG) underwent upper GI endoscopy. Mucosal inflammation, atrophic or malignant changes were evaluated histologically according to Sydney classification. Biopsies were taken from corpus and antrum. Genotyping of *H. pylori* was performed following microbiological cultivation. Expression of miR-155 was analyzed using TaqMan assay.

Results: MiRNA-155 expression was elevated in antrum mucosa of CG and AG compared to N ($p < 0.001$). H.pylori-negative CG was also associated with increased miR-155 expression, however, the highest expression was observed in H.pylori-related CG in both antrum and corpus ($p < 0.001$). Active infection with H.pylori was associated with higher miR-155 expression compared to patients with no H.pylori detection despite H.pylori-positive serology ($p < 0.05$). Expression of miR-155 was strongly dependent on cagA+ genotype and vacA status (s1i1 m1) ($p < 0.001$).

Discussion: Our data highlight the importance of H.pylori and miR-155 interaction. The magnitude of the miR-155 expression may be predictive for progression of H.pylori-triggered inflammation in gastric mucosa.

Abstract no.: W1.5

PROTON PUMP INHIBITORS ALTER GASTRIC MICROBIOTA COMPOSITION IN SUBJECTS WITH UPPER GASTROINTESTINAL SYMPTOMS: PRELIMINARY METAGENOMICS ANALYSIS

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Introduction and Aim: Human stomach harbours a broad variety of microorganisms, often evaluable only through metagenomics. Chronic therapy with PPIs increases the risk of gut microbiota-related diseases such as C. difficile infection and spontaneous bacterial peritonitis. Modification of gastric microbial ecosystem by PPIs has not been described yet.

Our aim is to assess the composition of gastric microbiota in subjects with upper gastrointestinal symptoms either taking or not PPIs.

Materials and Methods: We analyzed gastric biopsies from 10 consecutive patients undergoing upper endoscopy because of epigastric pain, heartburn or dyspepsia. We enrolled 5 patients taking PPIs (group A) and 5 ones free from gastrointestinal drugs (group B). We collected two biopsies for each patient. Roche 454 GS Junior was used for metagenomic analysis. Obtained data were analyzed by Qiime suite.

Results: Bacteria amplicons were detected in all samples. Overall, prevalent bacteria classes were Epsilonproteobacteria (26.5%), Bacilli (21%), Bacteroidia (19.3%), and Gammaproteobacteria (7.8%). Generally, a higher number of microorganisms was found in group A.

Differences in gut microbiota composition were observed between two groups. Higher abundance of Actinobacteria (9.74% VS 0.98%), Bacilli (27.78% VS 14.22%), Clostridia (8.96% VS 6.32%), Betaproteobacteria (7.68% VS 1.32%) and Gammaproteobacteria (13.86% VS 1.86%) and a lower presence of Epsilonproteobacteria (1.06% VS 51.8%) were found in group A when compared with group B.

Conclusions: PPIs modify gastric microbiota composition in subjects with upper gastrointestinal symptoms. Such phenomenon may explain the role of PPIs in gut-microbiota related diseases. Further investigations on this topic are warranted.

Abstract no.: W1.6

HIGH PREVALENCE OF MULTI-DRUG RESISTANCE IN *H. PYLORI* ISOLATES FROM 1001 NAÏVE PATIENTS

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Background: Antibiotic resistant strains of *H. pylori* have been increasing worldwide. Aim: to assess the prevalence of resistant strains to metronidazole, clarithromycin, and levofloxacin in naïve patients performing an EGDS for dyspeptic symptoms in Italy.

Methods: 1065 H.pylori infected naïve patients (median age: 51 years; IQR: 39–62) underwent gastroscopy and a biopsy sample was obtained to perform culture and an *in vitro* antimicrobial susceptibility testing. According to EUCAST 2012 guidelines, susceptibility testing was performed by epsilometer test.

Results: Data on resistance were available for 1001 patients (93.9%). Resistance to metronidazole was found in 38.3%; to clarithromycin in 32.7%; and to levofloxacin in 23.7% of the strains. Double resistance to clarithromycin + metronidazole was found in 10.4%; to clarithromycin + levofloxacin in 2.8%; and to metronidazole + levofloxacin in 5.6% whilst 10.4% of the strains were resistant to metronidazole + clarithromycin + levofloxacin.

Female sex was found to be related to both metronidazole resistance (OR: 2.5, 95% CI = 1.9–3.3; $p = 0.0001$) and metronidazole plus clarithromycin resistance (OR: 2.5, 95% CI = 1.5−4.0; $p = 0.0001$). An association with single metronidazole and clarithromycin resistance was found among non-Italian patients (OR: 2.0, 95% CI = 1.4−3.0; $p = 0.0001$ and OR: 1.8, 95% CI = 1.2–2.6, $p = 0.003$ respectively). No role for smoke, alcohol consumption and BMI emerged.

Conclusions: Resistant strains are widely prevalent in H pylori naïve patients. First line therapies need to account for increasing clarithromycin resistance. Levofloxacin based triple therapies are unlikely to represent an alternative front-line therapy.

Workshop 2 Therapy

Abstract no.: W2.1

PAN-EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): INTERIM ANALYSIS OF 5792 PATIENTS

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Introduction: Due to the diversity of *H. pylori* strains, resistances and geographical particularities, the most efficient management strategy is still to be found.

Aim: To systematically register the clinical practice of European gastroenterologists regarding *H. pylori* infection and treatment (31 countries, 250 recruiting investigators).

Methods: A Local Coordinator was selected from each country with more than 10 *H. pylori* references in PubMed. Each Coordinator selected a representative group of recruiting investigators from its country. An e-CRF was created to systematically register all adult patients infected with *H. pylori*. Variables included: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes (cure rates, compliance and follow-up).

Results: Up to now, 5792 patients have been included, and 3860 have finished follow-up. 58% females. 87% Caucasian. Mean age 57 years. 4.3% had drug allergies (77% to penicillin). 53% of indications were dyspepsia. 23% had gastroduodenal ulcer. 78% were treatment naïve, 16% second-line, 4.8% third-line, 1.2% fourth-line, and 0.5% fifth-line. Culture was performed in 15% (57% resistant). 63% of prescriptions were triple regimens, 12% non-bismuth quadruple concomitant, 14% sequential, and 6.9% bismuth-quadruple. 47% of patients had adverse events, although mostly mild (62%) and short (6.7 days), causing discontinuation in 4.2% of cases. Given the great diversity of included regimens, detailed results for first-line, rescue treatments, and adverse events will be presented as separate abstracts.

Conclusion: *H. pylori* management by gastroenterologists in Europe is extremely diverse, and in most settings suboptimal. Continuation of this registry may offer valuable information to improve this management.

Abstract no.: W2.2

A NEWLY DEVELOPED POTASSIUM-COMPETITIVE ACID BLOCKER, VONOPRAZAN VS. LANSOPRAZOLE IN FIRST-LINE TRIPLE THERAPY WITH AMOXICILLIN, AND CLARITHROMYCIN FOR *H. PYLORI* ERADICATION – PHASE 3, DOUBLE-BLIND STUDY

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Background: Vonoprazan (VPZ), a potassium-competitive acid blocker, has been shown to have a more potent acid-inhibitory effect than lansoprazole (LPZ) and consequently it was expected to have good efficacy compared with LPZ for *H. pylori* eradication.

Aims: To verify the non-inferiority of the efficacy of triple therapy with VPZ/amoxicillin (AMX)/clarithromycin (CLR) to that with LPZ/AMX/CLR in *H. pylori*-positive patients with gastric or duodenal ulcer history.

Methods: In this phase 3, randomized, double-blind, double-dummy, multicenter, parallel-group comparison study, eligible subjects were randomly allocated to one of four 7-day bid courses in the first-line therapy: VPZ (20 mg) or LPZ (30 mg), AMX (750 mg) and CLR (200 mg or 400 mg). VPZ/AMX/CLR and LPZ/AMX/CLR were compared regardless of CLR dose. Eradication was evaluated by the ^{13}C-urea breath test more than 4 weeks after the therapy.

Results: A total of 650 subjects were randomized. The eradication rate was 92.6% for VPZ/AMX/CLR and 75.9% for LPZ/AMX/CLR. The non-inferiority and superiority of VPZ/AMX/CLR to LPZ/AMX/CLR was confirmed (95% CI of difference [11.2%, 22.1%], $p < 0.0001$). Of note was that for subjects with CLR resistance, the eradication rate was significantly higher in VPZ/AMX/CLR compared with LPZ/AMX/CLR (82.0% vs. 40.0%, $p < 0.0001$). The overall incidence of drug-related treatment-emergent adverse events (TEAEs) was 20.4% in VPZ/AMX/CLR and 24.6% in LPZ/AMX/CLR. Most of the TEAEs were mild.

Conclusion: The non-inferiority and superiority of VPZ/AMX/CLR to LPZ/AMX/CLR was confirmed. Furthermore a significant difference was observed between VPZ/AMX/CLR and LPZ/AMX/CLR, especially in the subjects with CLR resistance. VPZ/AMX/CLR therapy was safe and well tolerated in this study.

Abstract no.: W2.3

A NETWORK META-ANALYSIS OF FIRST-LINE *H. PYLORI* ERADICATION REGIMENS

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Background: Given the difficulty of eradicating *H. pylori,* several first-line regimens have been proposed. Comparative studies and conventional meta-analyses are unable to answer which treatment offers the best global results. Network meta-analyses can provide and overall response to this question.

Aim: To evaluate the efficacy of all first line treatments using network meta-analytical methodology.

Methods: *Search strategy:* electronic searches on database and hand-search from bibliography from selected articles during a 25 year period. *Selection of studies:* full published papers of randomized clinical trials comparing any first-line treatment in *H. pylori* eradication reporting efficacy by intention-to-treat. *Methods:* network meta-analytical methodology using STATA-12 to estimate comparative OR, using both fixed and random effects models.

Results: Of 75 articles were selected for full review, and 62 were finally included (15 606 patients). Available regimens for network comparison were: Standard-triple (5, 7, 10 and 14-days), Bismuth-quadruple (7, 10 and 14-days), Sequential (10-days) and Concomitant (5, 7 and 10-days). Best overall results were achieved with Concomitant (7 and 10-day) and secondly with Bismuth-quadruple (10-day) regimens. Regarding 10 day regimens (Table), Standard-triple was significantly inferior to the rest. Sequential and Bismuth-quadruple were equivalent. Concomitant was significantly superior to sequential. Concomitant showed marginally non-significant higher efficacy than Bismuth-quadruple.

Conclusion: Network meta-analysis of *H. pylori* first-line treatments estimates best eradication results with 10-day concomitant and secondly with 10-day bismuth-quadruple regimens.

Table: Comparison of 10-day regimens

	Bismuth-quadruple	Sequential	Concomitant
Standard-triple	1.6 (1.2–2.1)*	1.6 (1.3–1.8)*	2.1 (1.5–2.9)*
Bismuth-quadruple		1.0 (0.77–1.3)	1.3 (0.9–2.0)
Sequential			1.4 (1.1–1.8)*

Numbers represent OR (95%C.I.) towards higher efficacy with the treatment in columns.
*Statistically significant

Abstract no.: W2.4

A RANDOMISED STUDY COMPARING 10 DAYS CONCOMITANT AND SEQUENTIAL TREATMENTS FOR THE ERADICATION OF *HELICOBACTER PYLORI*, IN A HIGH CLARITHROMYCIN RESISTANCE AREA

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Aims: Our study compares quadruple non-bismuth "concomitant" and "sequential" regimens for *H. pylori* eradication in a high clarithromycin resistance area.

Patients and methods: Multicenter prospective randomised clinical trial from Greece. We included *H. pylori* positive, treatment naïve, patients. All had positive CLO-test and/or histology and culture. They received either sequential (esomeprazole 40 mg, amoxicillin 1gr bid for 5 days, followed by 5 days of esomeprazole 40 mg, clarithromycin 500 mg and metronidazole 500 mg bid), or concomitant treatment (all drugs taken concomitantly bid for 10 days). Eradication confirmed by ^{13}C-urea breath test or histology 4–6 weeks after treatment. Adverse events and adherence were evaluated.

Results: One hundred ten patients (47F/63M, aged 19–83, mean 54 years, 38% smokers, 24% ulcer disease) allocated to concomitant and 109 (51F/58M, aged 21–94, mean 51.7 years, 33% smokers, 20% ulcer disease) to sequential treatment. Positive cultures 181/210 (86%), resistances: 35% metronidazole, 23% clarithromycin, 7.7% dual. Eradication rates were, respectively, 89.1% (98/110) versus 80.7%(88/109) by intention to treat ($p = 0.1$) and 93.4%(98/105) versus 83.8%(88/105) per protocol ($p = 0.04$, 95%CI:0.91–18.4). Overall, adherence was 98%(95%CI 95.9–99.6). Eradication rates according to resistances were: dual sensitive strains 44/44 (100%), 53/46 (94%) ($p = 0.4$), metronidazole single resistant 21/21 (100%), 21/28 (75%) ($p = 0.04$), clarithromycin single resistant 11/14 (79%), 11/14 (79%) ($p = 1$), and dual resistant 7/9 (78%), 2/5 (40%) ($p = 0.2$) for concomitant and sequential regimens, respectively. Side effects were reported by 40% of patients, comparable among regimens, and without treatment discontinuation.

Conclusions: Concomitant treatment eradication rate overcomes 90% per protocol and has a significant advantage over sequential therapy. This is probably due to its better efficacy on metronidazole resistant strains. Both regimens were well tolerated and safe.

Abstract no.: W2.5

TAILORED VERSUS BISMUTH QUADRUPLE VERSUS CONCOMITANT THERAPY FOR THE FIRST-LINE TREATMENT OF *HELICOBACTER PYLORI* IN CHINESE PATIENTS: A MULTICENTRE, OPEN-LABEL, RANDOMIZED CONTROL TRIAL

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Background: Empirical eradication therapies to *Helicobacter pylori* infection are often difficult to obtain satisfactory efficacy in China due to high prevalence of antibiotic resistance.

Aims: To compare eradication rate, safety and compliance among tailored, bismuth quadruple and concomitant therapy.

Methods: Consecutive dyspeptic patients referred for gastroscopy at three hospitals were recruited. 1050 patients with *Helicobacter pylori* infection and naïve to eradication were randomly assigned to 10-day tailored, bismuth quadruple and concomitant treatment. Tailored regimen was adjusted according to clarithromycin resistance (E-test) and CYP2C19 polymorphism (PCR to gastric mucosal samples). If clarithromycin-susceptible, PPI+amoxicillin (1 g bid)+clarithromycin (0.5 g bid); If clarithromycin-resistant, PPI+amoxicillin (1 g tid)+tinidazole (0.5 g tid). If homozygous-extensive-metabolizer, rebaprazole (10 mg bid); if heterozygous-extensive-metabolizer or poor-metabolizer, esomeprazole (20 mg bid). Bismuth quadruple regimen comprised esomeprozole (20 mg), amoxicillin (1 g), clarithromycin (0.5 g) and bismuth potassium citrate (220 mg), twice-a-day. Concomitant regimen comprised esomeprozole (20 mg), amoxicillin (1 g), clarithromycin (0.5 g) and tinidazole (0.5 g), twice-a-day.

Results: The three groups were well matched in basic information, antibiotic resistance and CYP2C19 polymorphism. Eradication efficacy was better in tailored group than other two groups in either ITT or PP analysis ($p < 0.05$). A higher rate of adverse events was recorded in concomitant treatment ($p < 0.05$) (Table 1).

Conclusions: Tailored therapy obtained a better efficacy and safety than bismuth quadruple and concomitant therapy in Chinese naïve patients with *Helicobacter pylori* infection, suggesting it may be a more suitable choice in regions with a high prevalence of antibiotic resistance.

Table 1: Comparison of *Helicobacter pylori* eradication rate, safety and compliance

	Tailored therapy (n = 350) (32 patients with negative cultures)	Bismuth quadruple therapy (n = 350)	Concomitant therapy (n = 350)
Eradication rate: ITT / PP analysis	88.7%/93.3%	77.4%/87.0%	78.3%/87.4%
Patients with adverse events	22.0%	26.6%	31.7%
Compliance (took at least 80% of drugs)	94.3%	90.0%	89.4%

Abstract no.: W2.6

TRIPLE THERAPY, SEQUENTIAL THERAPY, AND CONCOMITANT THERAPY FOR *HELICOBACTER PYLORI* INFECTION IN KOREA: A MULTICENTER, RANDOMIZED CONTROLLED TRIAL

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Background/Aims: Eradication of *Helicobacter pylori* infection with triple therapy (TT) has been reported to achieve unacceptable rates in Korea. The aim of this study was to compare the efficacy of sequential therapy (ST) and concomitant therapy (CT) with that of TT in Korea.

Methods: For this multicentre, randomized trial, patients with *H. pylori* infection from four centers in Korea were recruited. Patients were randomly allocated to TT (PPI, amoxicillin and clarithromycin for 10 days), ST (PPI and amoxicillin for the first 5 days, followed by PPI, clarithromycin and metronidazole for the next 5 days) or CT (PPI, amoxicillin, clarithromycin and metronidazole for 10 days).

Results: From March, 2013 a total of 227 patients were enrolled in our study. Seventy nine patients were allocated to the TT, 72 patients to CT group, and 65 patients to the ST group. For ITT analysis, the eradication rates of TT, ST and CT were 59.5% (47/79), 68.1% (49/72), 80.0% (52/65), respectively. For PP analysis, the eradication rates were 79.7% (47/59), 86.0% (49/57), 96.2% (50/52), respectively. CT achieved higher eradication rates than TT and ST. The rate of adverse events and adherence to the medication was similar between the three treatment groups.

Conclusions: Our prospective, multicenter study suggests that concomitant therapy may be better than triple therapy and sequential therapy for eradication of *Helicobacter pylori* in Korea. More data from more patients will be followed and this should allow us to reach more definite conclusions.

Workshop 3 Epidemiology and Paediatrics

Abstract no.: W3.1

ANTIMICROBIAL RESISTANCE OF *HELICOBACTER PYLORI* ISOLATES IN ALASKA NATIVE PERSONS FROM 2000 TO 2013: RESULTS FROM THE ALASKA SENTINEL SURVEILLANCE PROJECT

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Introduction: *Helicobacter pylori* (*H. pylori*) infection is more common in Alaska Native (AN) people than the general US population, with seroprevalence approaching 75%.

Methods: Gastric biopsy specimens were obtained from AN persons undergoing endoscopy for clinical indications between January 2000 and December 2013 at sites collaborating in CDC's sentinel surveillance system. Specimens were cultured to isolate *H pylori*. Susceptibility testing (agar dilution) for metronidazole [minimum inhibitory concentration (MIC) of resistant isolates: >8 μg metronidazole/mL], clarithromycin (MIC ≥1 μg/mL), amoxicillin (MIC ≥1), and tetracycline (MIC ≥2) was performed on *H. pylori* isolates from 593 persons and levofloxacin testing (Etest, MIC >2) was performed on isolates from 586 persons.

Results: *H. pylori* was isolated from 660/1521 (43%) persons undergoing upper endoscopy. Resistance to metronidazole was demonstrated in isolates from 46% of persons, clarithromycin 30%, amoxicillin 2%, and levofloxacin 15% of persons. Dual resistance to clarithromycin and metronidazole was observed in 15% of persons. Of those levofloxacin- resistant, 20% were also resistant to metronidazole and clarithromycin. Resistance to metronidazole (45–49%) and clarithromycin (24–39%) varied by region. Female patients were more likely than males to demonstrate metronidazole, and clarithromycin resistance ($p < 0.01$ both). A statistically significant increase in the proportion of persons with isolates resistant to levofloxacin was observed over time ($p < 0.01$).

Conclusion: Resistance to metronidazole, clarithromycin, and levofloxacin is common among *H. pylori* isolates from AN persons residing in Alaska. Persons infected with isolates demonstrating resistance to multiple antibiotics could have problems related to treatment and clearance of this infection.

Abstract no.: W3.2

THE PREVALENCE OF *HELICOBACTER PYLORI* REMAINS HIGH IN AFRICAN-AMERICAN AND HISPANIC VETERANS

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Helicobacter pylori prevalence in the United States has been declining albeit less in blacks and Hispanics. The aim of this study was to examine age- and race-specific prevalence rates of active *H. pylori* infection defined by culture and histopathology. This is a cross-sectional study performed at a Veteran Affairs medical center among patients scheduled for elective esophagogastroduodenoscopy (EGD) and from primary care clinics eligible for screening colonoscopy from 2008 to 2013. All underwent an EGD with gastric biopsies and completed a questionnaire. Samples were cultured irrespective of findings on histopathology. Positive *H. pylori* was defined as positive culture or histopathology (organism combined with active gastritis). We analyzed data on 1200 patients; most (92.8%) were men and non-Hispanic white (59.9%) or black (28.9%). *H. pylori* infection was positive in 347 (28.9%). Highest prevalence was in black males aged 50–59 (53.3%; 95% CI, 44.0–62.4%), followed by Hispanic males aged 60–69 (48.1%; 95% CI, 34.2–62.2%), and lowest in non-Hispanic white males aged 40–49 (8.2%; 95% CI, 2.7–20.5%). Those aged 50–59 were significantly associated with *H. pylori* positivity (adj. OR, 2.32; 95% CI, 1.21–4.45) compared with those aged 40–49, as were blacks (adj. OR, 2.57; 95% CI, 1.83–3.60) and Hispanics (adj. OR, 3.01; 95% CI, 1.70–5.34) compared with non-Hispanic whites. Those with some college education were less likely to have active *H. pylori* infection compared to those with no college education (adj. OR 0.51; 95% CI, 0.37–0.69). The prevalence of *H. pylori* remains high (28.9%) with higher rates in blacks and Hispanics with lower education levels.

Abstract no.: W3.3

H. PYLORI INFECTION RATE IS HIGHER BETWEEN THE THIRD AND THE FIFTH DECADE OF LIFE IN PATIENTS FROM LESS-INDUSTRILIZED COUNTRIES: A GOOD OPPORTUNITY FOR GASTRIC CANCER PREVENTION?

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Background: Epidemiological studies demonstrated how ethnicity might strongly influence the probability to acquire *H. pylori* infection. Rome is a multi-ethnic metropolis and many patients coming from less-industrialized Countries (LIC) come to our Gastroenterology Unit to perform 13C urea breath test (UBT) because of the occurrence of upper GI symptoms. The aim of this study was to assess the turnout of patients from LIC referred to our clinic and to compare the prevalence of *H. pylori* infection among patients from industrialized Countries (IC) and LIC.

Methods: Of 2482 patients (1621 female, mean age 46.5 ± 17.5 years) performed UBT between January 2013 and May 2014 in our Gastroenterology Unit according to international guidelines. 10.4% of them were from NIC, as assessed by the place of birth. Cumulatively, the studied population showed a DOB>3.50‰ in 25.1% of cases, with a statistically significant difference between patients from LIC compared to IC (38.9% versus 23.0% respectively, $p < 0.001$). Interestingly, when these results were pooled for age, a significant difference was maintained only in patients in the 3rd, 4th and 5th decade of age (46.9% versus 19.2%, $p = 0.001$; 50.8% versus 20.6%, $p < 0.001$; 38.1% versus 22.4%, $p = 0.007$ respectively).

Conclusions: Our data demonstrate that the prevalence of *H. pylori* infection is higher in patients form LIC but with a peculiar difference in the third, fourth and fifth decade of life. Those findings highlight the influence of sociocultural environment in the transmission of this infection and help to identify subpopulations who will benefit from *H. pylori* eradication to prevent gastric cancer.

Abstract no.: W3.4

H. PYLORI (HP) INFECTION WITH CAGA-POSITIVE STRAINS IS ASSOCIATED WITH ANAEMIA IN INFANTS AND TODDLERS

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Hp infection is considered to be one cause of iron-deficiency anaemia (IDA). Because infection is mainly acquired early in childhood, it is plausible that infected children are at increased risk of developing IDA as a consequence of hypochlorhydria associated with acute infection. However, the role of Hp virulence factors in paediatric anaemia is unknown. We evaluated whether infection by Hp CagA-positive strains is associated with anaemia in a longitudinal birth cohort of 116 children living in a poor community in Brazil. They were evaluated at 6, 12, 18, 24, 30 and 36 months of age. Children were considered Hp-positive when ^{13}C-UBT and monoclonal HpSA test, which have an excellent agreement to detect Hp infection, were both positive and Hp-negative when both tests were negative. CagA IgG serological status was evaluated by ELISA. Because maternal anti-CagA IgG may be present in young infants, analyses were undertaken after 12 months of age. Anaemia was strongly associated with Hp and CagA-seropositivity ($p < 0.001$) (Hp-pos/CagA-pos = 65.6%, Hp-pos/CagA-neg = 15.6%, Hp-neg/CagA-neg = 18.8%). Mean Haemoglobin-Hb and Haemotocrit-Ht values were significantly lower in CagA-seropositive than CagA-seronegative children at 12, 18 and ≥24 months of age ($p < 0.001$ for all). CagA IgG titres inversely correlated with the levels of Hb ($R = 0.38$, $p < 0.001$) and Ht ($R = 0.40$, $p < 0.001$). CagA seropositivity was considered a predictor of low levels of Hb/Ht in linear regression analyses ($t = -4.704$,-4.648, respectively, $p < 0.001$). Hb/Ht levels increased positively with increasing age in CagA-seronegative ($p < 0.001$), but not in CagA-seropositive children

($p = 0.40$). In conclusion, young children infected with CagA-positive Hp strains are at increased risk of developing anaemia.

Abstract no.: W3.5

EVOLUTION OF *HELICOBACTER PYLORI* ASSOCIATED GASTRO-DUODENAL ULCERS OR EROSIONS OVER THE LAST 23 YEARS: DECLINE OR STEADY STATE?

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Recent data suggest that, in children, the proportion of gastro-duodenal ulcers/erosions associated with *Helicobacter pylori* infection is currently lower than expected. In this study, we trace this proportion over two decades.

Methods: Retrospective review of the reports of all upper GI endoscopies with biopsies for culture over the last 23 years. *Helicobacter pylori* status was evaluated using a combination of several invasive methods and its rate compared in different time periods between children with lesions and controls

Results: A total of 7849 endoscopies were performed in 5983 children (2874F/3109M, median age 7.6 years, range 0.1–17.9 years). At their first endoscopy 12.2% of the children presented gastric and/or duodenal ulcers or erosions (35.4% of them infected by *Helicobacter pylori*) while no such lesions were identified in 87.8% (controls, 21.3% being infected). The exposure factors associated with such lesions were older age ($p < 0.001$), male gender (p 0.002) and *Helicobacter pylori* infection ($p < 0.0001$). Gastric ulcers were not significantly associated with *Helicobacter pylori* (23% infected) while only 55% of duodenal ulcers are associated with an infection, 33% of gastric erosions and 48% of duodenal erosions. The proportion of gastro-duodenal lesions associated with *Helicobacter pylori* remained stable over time. Children with *Helicobacter pylori* infection and ulcers were older than those with *Helicobacter pylori* without ulcers ($p < 0.001$).

Conclusions: Our study confirms that, in our paediatric population, the proportion of ulcers without *Helicobacter pylori* infection is higher than previously suggested and that this prevalence has not changed over the two last decades.

Abstract no.: W3.6

GAS PRODUCTION DURING LACTULOSE BREATH TEST IS ASSOCIATED WITH *HELICOBACTER PYLORI* INFECTION

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Background: Previous studies have shown that an impaired gastric acidity may increase the number of bacteria colonizing the GI tract and influencing gas production. Since *H. pylori* infection determines a variation of the gastric pH, we have designed a study aimed at assessing its possible role in intestinal gas production.

Methods: Of 101 consecutive patients (70 women, mean age 41 ± 15 years) that performed both a lactulose breath test and a ^{13}C urea breath test within 7 days in our Gastroenterology Unit between November 2013 and May 2014 were enrolled. All the tests were performed under standard conditions; Area Under the Curve (AUC) for produced H_2 and CH_4 was calculated with the trapezoidal rule; statistical analysis was performed using χ^2 test.

Results: 13 out of 101 patients (12.9%) produced more CH_4 than H_2 after 10 g lactulose ingestion, showing a AUC_{H2}/AUC_{CH4} ratio < 1. Among those, 53.8% obtained a DOB>3.50‰ at urea breath test, compared with 25% of patients with $AUC_{H2}/AUC_{CH4} > 1$ ($p = 0.032$). Moreover, we observed similar rates of small intestinal bacterial overgrowth (SIBO) in patients with and without *H. pylori* infection (13.8% versus 13.9%, respectively).

Conclusions: This study shows for the first time that more than a half of patients with a predominant methane production is *H. pylori*-positive, thus supporting the concept of an active interplay between *H. pylori* and intestinal microflora independently from the presence of SIBO. Finally, lactulose breath test could help identifying a subpopulation of patients with higher rates of *H. pylori* infection.

Workshop 4 Pathology

Abstract no.: W4.1

INFLAMMATORY RESPONSE IN NEONATAL THYMECTOMIZED BALB/C MICE INFECTED BY *HELICOBACTER PYLORI* STRAINS

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Recently, we described a cohort of thymectomized at day 3 post-birth (d3Tx) BALB/c mice infected with *H. pylori* that developed gastric MALT lymphoma (GML) lesions. This study aimed to investigate the pro-inflammatory response and to evaluate the regulatory T cell (Treg) compartment.

DNA and RNA were extracted from gastric biopsies of non-thymectomized (NTx) and d3Tx mice. DNAs were used for qPCR quantification of *H. pylori*. RNAs were used for chemokine and cytokine PCR array analysis and for qRT-PCR on IL-4, INFγ, lymphotoxin A and B. RNAs were also extracted from the spleen of NI mice and used for qRT-PCR targeting CD3 and Foxp3. The same experiments were performed on gastric biopsies from infected mice.

Th1 and Th2 cytokines were upregulated along with activators/regulators of the lymphoid response and numerous chemokines. IL-4, INFγ, LTa and LTb were significantly upregulated when considering all the d3Tx mice *versus* NTx in correlation with the inflammatory scores. Higher Foxp3/CD3 ratios were found in the spleen of NI d3Tx mice which indicates an enrichment of Tregs following thymectomy. Higher quantities of T cell and Treg infiltrations were found in the stomach of infected d3Tx mice versus NTx, again correlated with inflammatory scores. There was a higher level of *H. pylori* colonization in NTx versus d3Tx mice. In d3Tx mice this was inversely correlated with inflammatory scores.

GML lesions in *H. pylori*-d3Tx infected mice are associated with an increase in local pro-inflammatory cytokines and chemokines. Collectively our data suggest that Tregs support the inflammation process.

Abstract no.: W4.2

HELICOBACTER PYLORI ACTIVATES C-TYPE LECTIN, MINCLE: YET ANOTHER SURVIVAL STRATEGY?

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The survival of *H. pylori* in human stomach is due to its ability to modify and evade the activated (innate) immune system as well as adaptive immunity by modulation of effector T cell functions. In addition to Toll Like Receptors (TLRs) and Nucleotide Oligomerization Domain Protein (NOD), *H. pylori* possesses domains for C- type Lectin Receptors (CLRs), notably Mincle (Macrophage Inducible C- type Lectin). The latter is predominantly expressed on activated macrophages and recognizes various ligands such as mycobacteria, fungi, yeast and dying cells.

However, there are no reports about recognition of Mincle by *H. pylori*. We studied the role of Mincle in *H. pylori* mediated immune response. Cultured human macrophage (THP-1) cells were infected with *H. pylori* wherein strong up-regulation of Mincle mRNA was observed and confirmed by qRT-PCR. In addition, heat killed *H. pylori* also induced Mincle mRNA expression, hinting that Mincle may not recognize protein determinant (s) but rather detects carbohydrate domains. Furthermore, blocking of Mincle receptors and knocking down of Mincle gene by siRNA transfection in macrophages showed significant decrease in IL-10 and an increase in TNF-alpha mRNA expression and secretion, respectively. These results suggest that, *H. pylori* resorts to an efficient mechanism for its persistence by activating Mincle expression thereby avoiding strong proinflammatory response and recognition by adaptive immune system.

Abstract no.: W4.3

HELICOBACTER PYLORI GROWTH IS ASSOCIATED WITH ALTERED IRON HOMEOSTASIS IN AGS CELLS

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Helicobacter pylori infection is widely associated with systemic iron deficiency in humans. It remains to be determined whether these bacteria elicit a similar response in gastric epithelial cells. However, this seems unlikely as *H. pylori* need to acquire iron to survive. Ferritin is a protein that stores iron in cells. Accordingly, this study investigated the expression of ferritin in AGS cells (a gastric epithelial cell line) in response to *H. pylori* infection.

Western blotting and immunofluorescence microscopy identified that ferritin levels are very low in uninfected AGS cells. However, when cells were exposed to low number of *H. pylori* (MOI 10:1) for 15 hours, ferritin expression was found to increase ($p < 0.001$; paired t-test) and correlated with an increase in total cellular iron content, as measured by the ferrozine assay. This increase in total iron independent of extracellular concentrations of iron must be explained by *H. pylori*-induced alterations in the control mechanism of iron homeostasis in the AGS cells.

A redistribution of labile iron from the cytosol to the lysosomes was also found, which is intriguing because these compartments are considered the site of intracellular ferritin degradation. Moreover, an increase in lysosomal iron correlated with enhanced *H. pylori* growth and increased cellular vacuolation. Collectively these findings suggest a previously undescribed mechanism that enables *H. pylori* to obtain the iron they require for survival from the host epithelium.

Abstract no.: W4.4

ROLE OF CAGA-POSITIVE STRAINS OF *H. PYLORI* IN ACUTE MYOCARDIAL INFARCTION WITH ST-SEGMENT ELEVATION

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We have previously shown a significant association between CagA-positive strains and non-ST elevation myocardial infarction. Therefore, we have designed a study aimed at assessing the prevalence of CagA-positive strains in patients with ST-elevation myocardial infarction (STEMI) and of recurring acute coronary syndromes (ACS) and the usefulness of the assessment of serum levels of anti-CagA IgG as an outcome predictor in patients with STEMI .

Methods: We enrolled 181 patients with STEMI and 50 matched healthy controls. In all patients, serum levels of IgG anti-CagA and anti-HAV were assessed. A previous history of ACS and the rate of major adverse cardiovascular events (MACEs) were evaluated with a 2 years follow-up.

Results: CagA-positive strains were significantly higher in STEMI patients compared to controls (33.1% vs 9%, $p = 0.026$). Moreover, anti-CagA antibody titer was significantly increased in STEMI patients compared to controls (62.7 ± 39 vs 25.6 ± 42.7, $p = 0.02$). Interestingly, patients with STEMI and a previous history of ACS had an higher prevalence of CagA-positive strains (50% vs 29.3%, $p = 0.019$) and higher antibody serum levels (97.5 ± 50.4 vs 55.2 ± 25.3, $p = 0.001$). Furthermore, MACEs rate was significantly higher in patients infected by CagA-positive strains (LogPrank = 0.014). Finally, there was a negative correlation between levels of anti-HAV and anti-CagA IgG ($R = 0.271$, $p = 0.11$) thus excluding an aspecific bystander activation.

Conclusions: CagA-positive strains of *H. pylori* may be involved in the pathogenesis of STEMI and in the recurrence of ACS. Serum assessment of IgG anti-CagA may be an useful tool for risk stratification in patients with STEMI as they may positively predict MACEs rate.

Abstract no.: W4.5

PRIMARY GASTRIC LYMPHOMA DETECTED BY SCREENING UPPER ENDOSCOPY IN HIGH PREVALENCE AREA OF *HELICOBACTER PYLORI* INFECTION

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Background/Aims: This study aimed to identify the clinical characteristics and prognosis of primary gastric lymphoma detected by screening upper endoscopy in high prevalence area of *Helicobacter pylori* (*H. pylori*) infection.

Methods: Between October 2003 and May 2013, consecutive subjects who were diagnosed with primary gastric lymphoma by screening upper endoscopy were retrospectively enrolled at Seoul National University Hospital Healthcare System Gangnam Center, Seoul, Korea.

Results: During the study period, a total of 101 103 subjects received 207 114 screening upper endoscopy. Among them, primary gastric lymphoma was detected in 49 subjects. They were 53.0 ± 10.5 years of age, and 72.9% (35/49) were female. Histologic type of primary gastric lymphoma was predominantly (98.0%, 48/49) extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma), and one remaining case (2.0%) was diffuse large B-cell lymphoma. Initial stage was IEa in 95.9% (47/49), and *H. pylori* was positive in 91.8% (43/49). Among 41 *H. pylori*-positive patients with gastric MALT lymphoma stage IEa, *H. pylori* eradication achieved complete remission in 95.1% (39/41). There were three cases of recurrence with (n = 2) or without (n = 1) reinfection of *H. pylori*.

Conclusions: Upper endoscopy as a screening for upper gastrointestinal malignancy may detect gastric MALT lymphoma in early stage, which can be successfully treated with *H. pylori* eradication, especially in *H. pylori* endemic area. For those who achieved complete remission, it is needed to undertake surveillance for recurrence.

Abstract no.: W4.6

SERUM PEPSINOGENS FOR DETECTION OF FUNDIC GASTRIC ATROPHY IN SUBJECTS WITH AUTOIMMUNE THYROID DISEASE

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Background: Autoimmune gastritis (AIG) leads to fundic gastric atrophy (FGA), a condition that increases the risk for gastric cancer. The prevalence of AIG is high among subjects with autoimmune thyroid disease (ATD).

Aim: In this case-controlled study we evaluate the usefulness of serum pepsinogens for screening of FGA among subjects with ATD.

Methods: Patients with known or newly diagnosed ATD (cases) and goitre (controls) presenting to the Otto-von-Guericke University Hospital from October 2012 to Februar 2014 were enrolled in the study. Pepsinogen (PG)-I levels ≤25 μg/mL and PGI/II ratio ≤3 were indicative for FGA. Serum anti-*Helicobacter pylori* (*H. pylori*) IgG antibody titers were also determined. Upper endoscopy was offered to subjects with serological FGA and histological FGA stage was assessed by OLGA.

Results: Of 29 patients with ATD (21 with Hashimoto thyroiditis and 8 with Graves' disease), and 28 controls with goitre were enrolled. The majority of subjects were female, and subjects with ATD were younger than controls (mean age 54.7 ± 13.7 and 67.2 ± 13 years, respectively, $p < 0.05$). Prevalence of *H. pylori* infection in cases and controls was 17.2% and 25.5%, respectively. Serological FGA was present only in cases with ATD (7/29, 24.1%). One patient with FGA had serological evidence of *H. pylori* Infection. In all cases FGA was confirmed by histology. OLGA stage was II and III in 5 and 2 cases, respectively.

Conclusions: Serum pepsinogens are useful for serological screening of FGA among patients with ATD and may have an impact on patient management.

Workshop 5 Gastric Cancer

Abstract no.: W5.1

THE DECREASING INCIDENCE OF GASTRIC MALT LYMPHOMA AND *HELICOBACTER PYLORI* TREATMENT

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Helicobacter pylori (Hp) plays a pivotal role in gastric MALT lymphoma (GML) and regression is obtained with antibiotics in most cases. Since 1992 Hp treatment as first line therapy for GML and for dense lymphoid infiltrates gastritis was devised in our hospital. By the time a dramatic reduction of GML incidence was noticed.

Aim of this study is verifing this drop over 20 years and its link to Hp eradication. The rates of Hp+vity and GML were compared during three 3-year periods and data of follow up were compared.

New GML decreased from 0.23% (38 in 1992–1994) to 0.08% (9 in 2002–2004) and to 0.05% (10 in 2010–2012) while Hp+vity from 49% to 32% and to 20%. Incidence of GML during the first interval dropped more than expected on the base of Hp+vity decline. Both drops remained aligned during the second interval. The subset of new GML resistant to Hp eradication remained unmodified. The proportion of Hp-ve GML increased from 1/38 to 4/10. In contrast to GML, the incidence of non-Hodgkin lymphomas is stable in our Cancer Registry.

The effect of Hp eradication is obvious. Disproportioned GML drop during the first interval could also be caused by the introduction of proton pump inhibitors, with consequent downfall of bacterial concentration. Eradication of Hp in all cases with dense lymphoid infiltration, could explain both the initial disproportionate drop and the tendency to select cases either Hp-ve or resistant to antibacterial treatment.

Abstract no.: W5.2

IL1B SIGNALING LEADS TO INCREASED CELL SURVIVAL OF GASTRIC CARCINOMA CELLS

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Polymorphisms in inflammation-related genes have been associated with risk to gastric carcinoma (GC). However, the biological mechanisms underlying these associations are still elusive. Our objective was to determine whether chronic inflammation-associated IL1B signaling, as seen in the context of *Helicobacter pylori* infection, can be linked to gastric carcinogenesis by modulating the behaviour of gastric epithelial cells.

The effect of IL1B was assessed by studying the expression and activation status of the IL1B-activated transcription factors C/EBPβ and CREB in GC cell lines. Interaction between CREB and C/EBPβ was explored through interference RNA, chromatin immunoprecipitation and chemical inhibition. CREB and C/EBPβ expression was analyzed in 66 samples of primary GC and in normal gastric mucosa. GC cells growth was analyzed *in vitro* by BrdU incorporation and *in vivo* employing a chicken embryo chorioallantoic membrane model.

We found that IL1B regulates the expression/activation status of both C/EBPβ and CREB in GC cells through an ERK1/2-dependent mechanism. Our results show that CREB is a direct transactivator of *CEBPB*, acting as an upstream effector in this regulatory mechanism. Furthermore, we found CREB to be overexpressed in 94% of GC samples and significantly associated with C/EBPβ expression ($p < 0.05$). Finally, we demonstrate both *in vitro* and *in* vivo that CREB can mediate IL1B-induced GC cell proliferation.

Our results support the hypothesis that the effect of chronic inflammation on gastric carcinogenesis, as seen in the context of genetically susceptible individuals infected with *H. pylori*, includes modulation of signaling pathways that regulate survival mechanisms in epithelial cells.

Abstract no.: W5.3

HELICOBACTER PYLORI INFECTION AND GASTRIC MUCIN EXPRESSION IN FIRST DEGREE RELATIVES OF GASTRIC CANCER SUBJECTS

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Introduction: There are currently no guidelines for the surveillance of first degree relatives (FDRs) of gastric cancer patients. *Helicobacter pylori* (Hp) related intestinal metaplasia (IM) is a risk factor for future gastric cancer, and may be associated with altered mucin expression at an early stage. This could potentially aid in the early detection of gastric cancer.

Methods: FDRs and controls were prospectively recruited and underwent upper endoscopy. Biopsies were taken according to the OLGA/OLGIM protocol. Hp infection was tested with giemsa stain and serology. Immunohistochemistry staining for MUC1, MUC2, MUC5AC and MUC6 was performed. Serum pepsinogen-I and pepsinogen –II were assayed.

Results: Of 40 FDRs and 8 controls were included; mean age 46.7 ± 12.0 years. Endoscopy was normal in all FDRs and controls. Histological gastritis was present in 23(57.5%) FDRs and 5(62.5%) controls (p = ns). Glandular atrophy, IM and dysplasia were absent in all FDRs and controls. There was no difference in Hp infection (14(35%) and 2(25%) FDRs and controls, respectively ($p = 0.46$)). Superficial MUC1 expression was significantly increased in FDRs (47.5% vs. 0%; $p = 0.01$).There was no difference in the expression of deep MUC1, MUC2, MUC5AC or MUC6. Mean pepsinogen-I was 95.61 ± 55.43 μg/L and 90.05 ± 34.35 μg/L in FDRs and controls, respectively ($p = 0.79$). The ratio of pepsinogen-I to pepsinogen-II was 11.98 ± 3.75 μg/L and 15.08 ± 5.82 μg/L in case and controls, respectively ($p = 0.06$).

Conclusion: Despite normal appearing mucosa and the absence of intestinal metaplasia by histology, FDRs of gastric cancer patients exhibit increased expression of MUC1 which may serve as a predictor for future IM, dysplasia and cancer.

Abstract no.: W5.4

PATTERN RECOGNITION RECEPTORS IN *HELICOBACTER PYLORI*-RELATED GASTRIC CANCER

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Introduction: Toll-like receptors (TLRs) and NOD-like receptors (NLRs), two subtypes of pattern recognition receptors (PRRs), are ancient innate immune mechanisms that are linked by mutual regulation and are critical for generating pro-inflammatory cytokines. Because *Helicobacter pylori*-related gastric cancer (GC) is a progressive process initiated by inflammation, we investigated the role of PRRs in gastric carcinogenesis.

Methods: Seventy-six polymorphisms were detected by PCR, real-time PCR and MALDI-TOF mass spectrometry in 310 ethnic Chinese individuals (87 non-cardia GC cases/223 controls with functional dyspepsia). Gene expression of 84 molecules involved in the NLR signalling pathway was assessed through quantitative PCR in mammalian cells challenged with *H. pylori* GC026 (GC) and 26695 (gastritis).

Results: On multivariate analysis, *TLR4*-rs11536889 and *CARD8*-rs11672725 remained statistically significant. Statistical analyses assessing the joint effect of *H. pylori* infection and the selected polymorphisms (*TLR2, TLR4, MD-2, LBP, TIRAP, CARD8, NLRP3, NLRP12, NLRX1* and *CASP1*) revealed strong associations with GC. In gene expression analyses, five genes encoding NLRs were significantly regulated in *H. pylori*-challenged cells (*NLRC4, NLRC5, NLRP9, NLRP12* and *NLRX1*). Interestingly, *NLRP12* and *NLRX1*, two known NF-κB negative regulators, were markedly down-regulated, while *NFKB1* and several NF-κB target genes encoding pro-inflammatory cytokines, chemokines and molecules involved in carcinogenesis, were up-regulated in *H. pylori* GC026-challenged cells.

Discussion: Novel associations between polymorphisms in the TLR and NLR signalling pathways and GC were identified in Chinese individuals, a high GC risk population. Our gene expression results highlight the relevance of the NLR signalling pathway in gastric carcinogenesis and its close interaction with NF-κB.

Abstract no.: W5.5

EXPRESSION OF ALDEHYDE DEHYDROGENASE DEFINES CANCER STEM CELL POPULATION IN GASTRIC CARCINOMA

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Gastric cancer is the fifth most common cancer in frequency and the second leading cause of cancer mortality in the world. Research on stem cells in gastric carcinoma have encountered the lack of specific markers for the identification and isolation of cancer stem cells (CSCs). A recent study conducted mainly on gastric cell lines has proposed CD44 as a marker for the identification of gastric CSCs (Takashi et al, 2009). The overall aim of our work is to clarify the characterization of CSCs in primary gastric tumors to identify specific CSC markers and new potential therapeutic targets. Our studies using flow cytometry evaluated 11 putative CSC markers described in other cancers in five primary gastric tumors and five gastric cancer cell lines. Among the markers expressed in a smallest number of cells, we found CD105, CD166 and ALDH which are expressed at a low level (<20%). We also analyzed the ability of cell subpopulations sorted by FACS to express CD105, CD73, CD90, CD166 or ALDH and form tumorspheres *in vitro*. Our results indicated that ALDH+ cells have a strong ability to form tumorspheres compared to other FACS-sorted cells. Finally, *in vivo* studies of tumorigenicity by xenograft experiments in immunodeficient mice confirmed that ALDH+ cells are able to form gastric tumors but not ALDH- cells. These results suggest that ALDH can be considered as a more selective marker of tumor-initiating CSCs in gastric adenocarcinoma than CD44.

Abstract no.: W5.6

THE ROLE OF PTEN/FAK SIGNALING PATHWAYS IN THE PATHOGENESIS OF *HELICOBACTER PYLORI*-ASSOCIATED GASTRIC CANCER

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Background: PTEN (phosphatase and tensin homolog) is a tumor suppressor gene, which encodes a dually functional phosphatase with lipid and protein phosphatase activities. *Helicobacter pylori* infection plays the important role in the development of gastric carcinoma, but how influences the mechanism by PTEN/FAK signaling pathway is not clear.

Methods: A total of 160 tissue specimens of chronic non-atrophic gastritis, intestinal metaplasia, dysplasia and gastric cancer. (20 *H. pylori*-positive and 20 *H. pylori*-negative, respectively) were recruited for immunohistochemical analysis of PTEN, phosphorylation of PTEN (p-PTEN), FAK, and phosphorylated FAK (p-FAK) expression. Build different gastric epithelial cell lines with overexpression of PTEN protein, GES-1, GES-1-Empty, GES-1-PTEN-WT or GES-1-PTEN-MT cells were incubated with *H. pylori* at a MOI of 50. After incubation for 1 hour, cell lysates were detected expression of PTEN/FAK related proteins using Western blot. At 20 hours, invasion cells were counted by Transwell assay.

Results: Overall, the expression of PTEN was progressively decreased from chronic non-atrophic gastritis to gastric cancer, and p-PTEN increased. FAK and p-FAK expressions were also showed the increased trends. In chronic non-atrophic gastritis, p-PTEN expression was significantly higher after *H. pylori* infection. In GES-1, GES-1-Empty, GES-1-PTEN-WT and GES-1-PTEN-MT, *H. pylori* could induce a significant increase of PTEN phosphorylation and p-FAK expression. We found the numbers of cell invasion were significantly increased in *H. pylori* infection group.

Conclusions: *H. pylori* could induce a significant increase of PTEN phosphorylation and decrease of phosphatase activities, activating its downstream effector FAK to improve the cell invasive ability at the early stage.

Workshop 6 Extradigestive and Others

Abstract no.: W6.1

DOES *HELICOBACTER PYLORI* INFECTION IMPACT THE COURSE OF ALZHEIMER'S DISEASE? AN ANIMAL STUDY

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Background: *Helicobacter pylori* infection seems to play a critical role in extragastric diseases including Alzheimer's dementia (AD). Chronic *H. pylori* infection could worsen AD lesions *via* atherosclerosis and inflammation. Our aim was to determine the impact of *Helicobacter* species infection on cerebral lesions and behaviour of AD transgenic (Tg) mice and their wild type (WT) littermates.

Methods: Tg mice (APPswe/PS1dE9) and their WT littermates were infected with *H. pylori* (n = 60) or *Helicobacter felis* (n = 60) or left uninfected (n = 60). Cognitive performances (Y-maze, open field, novel object location and direct social interaction) and histological abnormalities were evaluated at 4, 6 and 10 months of age. Brain specimens were processed to detect cerebral amyloid plaques (thioflavin-S stain) and astroglial and microglial cells (immunochemistry anti-GFAP and anti-iba-1, respectively). Stomach specimens were processed to detect gastric lesions (hematoxylin and eosin stain).

Results: *H. pylori* did not lead to any histological or behavioural consequences at 4 months of age, however, at 6 and 10 months of age, it was associated with an increased number of amyloid plaques in Tg mice but without any change in behaviour. At 10 months of age, Tg mice had impaired cognitive and social behaviour with a higher neuroinflammation (immunochemistry and q-PCR) than WT littermates.

Conclusion: *H. pylori* infection was associated with an increased number of brain amyloid plaques, but not with increased neuroinflammation or behavioural change at 6 and 10 months of age. More studies are needed to firmly conclude that there is an association between *H. pylori* infection and AD.

Abstract no.: W6.2

DIVERSITY OF THE GASTRIC MICROBIOTA IN *H. SUIS*-INFECTED AND *H. SUIS*-NEGATIVE SLAUGHTERHOUSE PIGS

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Helicobacter suis infection is an important cause of gastric disease in pigs and humans. This bacterium is found in the majority of pigs worldwide, but little is known on the presence of other microorganisms in the stomach of these animals. In this study, we aimed at analyzing the porcine gastric microbiota and at investigating differences of the gastric microbiota in *H. suis*-positive and *H. suis*-negative pigs. Quantitative PCR was performed on DNA extractions of gastric biopsies from slaughterhouse pigs to determine *H. suis* positivity. Subsequently, 6 *H. suis*-positive and 6 *H. suis*-negative animals were selected for further analysis. After amplification of 16S rRNA genes from the bacterial population, sequencing was performed using the Genome Sequencer Junior System (Roche 454 Life Sciences). Although the microbiota was diverse and differed between animals, the most frequently detected bacteria were *Fusobacterium spp*. (including a putative new species), *Lactobacillus spp*., *Campylobacter spp*. and *Escherichia coli*. The number of *E. coli* bacteria was higher in the stomach of *H. suis*-positive pigs compared to *H. suis*-negative pigs, whereas more *Campylobacter jejuni* bacteria were present in *H. suis*-negative animals. Further *in vitro* experiments showed that growth of both *E. coli* and *C. jejuni* is stimulated when co-incubated with *H. suis* bacteria. Interestingly, both *E. coli* and *C. jejuni* were able to suppress the growth of *H. suis*. Further research is needed to obtain a better insight into the interactions of *H. suis* with other bacteria and their effects on gastric health.

Abstract no.: W6.3

SEROLOGICAL ASSOCIATION OF *HELICOBACTER PYLORI* PROTEINS AND BILIARY TRACT CANCER IN THE ATBC STUDY

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Background: *Helicobacter species* have been detected in human bile and hepatobiliary tissue. Despite evidence that they promote gallstone formation and hepatobiliary tumors in laboratory studies, their contribution to these cancers in humans remains unclear.

Methods: To assess *H. pylori* association with subsequent incidence of hepatobiliary cancers in the Finnish Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) study we used multiplex serology, a bead-based assay (Luminex) enabling simultaneous and quantitative detection of antibodies against 15 different *H. pylori* proteins. 64 biliary cancers, 122 liver cancers, and 224 age-matched controls occurring over the course of 22 years were included. *H. pylori* seropositivity was defined as seropositivity to ≥4 antigens. Odds ratios (OR) and 95% confidence intervals were adjusted for major hepatobiliary cancer risk factors.

Results: Among controls, 88% were *H. pylori* seropositive at baseline. Among those who subsequently developed hepatobiliary cancer, prevalence of seropositivity was higher: 100% for gallbladder cancer, 97% of extrahepatic bile duct cancer, 91% of Ampulla of Vater cancer, 96% of intrahepatic bile duct cancer, and 94% of hepatocellular carcinoma. The OR for all biliary tract cancers combined was 5.47 (95%CI: 1.17–25.65). Four antigens were associated with this combined endpoint: GroEl (2.14; 1.00–4.58), UreA (3.06; 1.54–6.08), HP0305 (1.98; 1.06–3.70), and Omp (3.94; 1.57–9.87). The OR for seropositives for these four antigens was 9.07 (1.05–78.69) relative to those seronegative for all four. *H. pylori* seropositivity was not associated with hepatocelullar carcinoma (1.20; 0.42–3.45).

Conclusions: Seropositivity to *H. pylori* proteins was associated with increased risk of biliary tract cancers in ATBC.

Abstract no.: W6.4

INFLUENCE OF GASTROINTESTINAL MICROBIOTA ON PATHOGENIC POTENTIAL OF *HELICOBACTER PYLORI* IN C57BL/6 MICE

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The gastrointestinal microbial communities of C57BL/6 mice between Taconic Farm (Tac) and Jackson Laboratory (Jax) are highly variable; most notably, only the Tac mice are colonized with segmented filamentous bacteria (SFB), a potent inducer of proinflammatory TH17 cells. To examine whether Jax and Tac mice have a different intestinal microbiome and respond differently to Hp infection, C57BL/6 mice from Tac and Jax were dosed with Hp PMSS1. As measured by Illumina sequencing, OTUs in fecal microbiomes were richer in Tac than Jax mice ($p < 0.01$); the ratio of Bacteriodetes to Firmicutes, two predominant phyla, were 1.86 for Jax but 0.33 for Tac mice. By 16 week-post-inoculation, Hp levels, mRNA expression of gastric Il-1β, Il-17A and RegIIIg were significantly lower in Tac compared to Jax mice ($p < 0.05$). Gastric pathology in the infected groups was more severe compared to the controls ($p < 0.0001$) but there was no significant difference between the infected Tac and Jax mice. Additionally, Hp infection in Tac mice increased SFB levels in the large intestine but did not influence ileal SFB levels compared to the controls. Interestingly, Hp infection significantly altered fecal microbial compositions of Tac mice with an increase of the class Bacilli and a decrease of the classes Clostridia and Bacteroidia but not noted in Jax mice. Our data indicate that the gastrointestinal microbiomes in Tac mice are more diverse and prone to Hp perturbation compared to Jax mice. Long-term clinical effects of different responses to Hp infection between Jax and Tac mice need to be further elucidated.

Abstract no.: W6.5

HELICOBACTER PYLORI AND PREECLAMPSIA: ROLE OF ANTI-CAGA ANTIBODIES ON PLACENTAL DEVELOPMENT

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Preeclampsia (PE) is a severe hypertensive pregnancy-related disorder that affects 5–8% of women worldwide. The etiopathogenic mechanisms of PE are still poorly understood and current leading hypotheses rely on disturbed placental function in early pregnancy.

Previous studies have found the association between subclinical infections with CagA-positive *Helicobacter pylori* (HP) strains and the onset of PE.

To investigate the pathogenic role of HP in PE, blood samples from 78 pregnant women with PE and 87 women with uneventful pregnancies were collected and analysed for anti-Urease B and anti-CagA antibodies positivity (ELISA, immune-blot). A significantly higher percentage of HP seropositive women was found among PE cases (65.4%) compared to controls (33.3%, $p < 0.001$). The difference was even greater for anti-CagA seropositivity (44.4 and 13.7%, respectively, $p < 0.001$).

To evaluate whether anti-CagA antibodies may recognize antigens at maternal and/or fetal site of developing placenta, polyclonal IgG fraction from high titer anti-CagA positive PE patients' sera and commercial monoclonal anti-CagA antibody were tested on human primary trophoblast cultures and Human Endometrial Endothelial Cells (HEEC) cultures.

Monoclonal and polyclonal anti-CagA antibodies were found to: i) bind to human trophoblast cells (ELISA, immunofluorescence) impairing trophoblast invasiveness in vitro (3D invasion assay commercial kit); ii) bind to HEEC decreasing the number and the total length of the tubules formed in vitro; iii) reduce in vivo angiogenesis in subcutaneous angioreactors in a murine model.

This is the first work suggesting a role for CagA positive HP infection in the etiopathogenesis of PE through a mechanism of anti-CagA antibody-mediated placental impairment.

Abstract no.: W6.6

SEMEN LEVELS OF INTERLEUKIN-6 AND TUMOUR NECROSIS FACTOR-α ARE INCREASED IN CAGA POSITIVE *H. PYLORI* INFECTION AND MAY CAUSE SPERM ALTERATIONS

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Introduction: *Helicobacter pylori* infection adversely influences the reproductive sphere both in women and men. In men, when the infection is caused by strains expressing CagA, we observed reduced fertility and sperm alterations, such as decreased motility and increased number of unviable sperm.

Patients and Methods: In 109 selected individuals attending our Department for semen analysis, we investigated serologically *H. pylori* infection and the CagA status by Western blotting. Semen analysis was performed following WHO guidelines (2010); apoptosis and necrosis of spermatozoa were determined by Vybrant apoptosis assay; semen IL-6 and TNF-alpha levels were determined by ELISA.

Results: Twenty-eight out of 109 subjects (25.6%) were infected by *H. pylori* (HP+); among the 28 infected men, 12 men (42.8%) were CagA seropositive (CagA+) and 16 were seronegative (CagA-); 81 subjects were seronegative (HP). Semen concentrations of TNF-alpha and IL-6 were increased in HP+ vs. HP- group (TNF-alpha 41 pg/mL vs 27 pg/mL; IL-6: 11 pg/mL vs 5 pg/mL, $p < 0.01$). Respect to HP- group, CagA + group showed reduced sperm motility (24% vs. 32%, $p < 0.05$), enhanced necrosis (33.5% vs. 21%, $p < 0.05$) and inflammatory cytokines levels (TNF-alpha 46 pg/mL vs 27 pg/mL, $p < 0.01$; IL-6: 17.5 pg/mL vs 5 pg/mL, $p < 0.01$). In the CagA+ group, sperm motility was lower vs. CagA- group (24% vs. 36.5%, $p < 0.05$).

Discussion: This study shows that CagA+ *H. pylori* infection increases the semen levels of inflammatory cytokines, which may determine sperm injury and therefore contribute to decrease the reproductive potential in men.

POSTERS
P01 Microbiology

Abstract no.: P01.01

INTERLABORATORY EXTERNAL QUALITY CONTROL FOR IDENTIFICATION AND ANTIBIOTIC SUSCEPTIBILITY TESTING OF *HELICOBACTER PYLORI* BY CULTURE AND BY MOLECULAR METHODS

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Background: Quality standards and compliance to the international ISO15189 requirements for quality and competence of medical laboratories is becoming mandatory in most countries in Europe. We aimed to assess the performance of three microbiology laboratories (in Belgium, France, and Portugal) in an external quality control (EQC) for identification (ID) and antibiotic susceptibility testing (AST) of *Helicobacter pylori* by culture and by molecular methods.
Methods: Two EQC sessions consisting of sending a panel of 10 culture isolates and 10 bacterial DNA extracts for the detection of *H. pylori* were organized in 2013. Each laboratory processed the specimens blindly using their own in house methods. Results were analyzed for concordance between labs for culture, ID, AST, and by molecular methods (RT-PCR or PCR-reverse hybridization assay) for the detection of 23S rRNA mutations associated with resistance to macrolides. Discordant results were resolved following a separate reanalysis of the samples.
Results: Interlaboratory agreement was 100% for culture, 96–100% for phenotypic tests, 90–100% for ID and 92–100% for AST. Concordant results were obtained in 80–100% for the detection of macrolide resistance mutations. Reanalysis of discordant results confirmed the initial categorization suggesting that the discrepancies were not due to technical issues but rather to incorrect labelling of the specimens during processing.
Conclusions: Overall, excellent Interlaboratory agreement was observed, hence validating the phenotypic and genotypic diagnostic methods of *H. pylori* in the three laboratories. Following these promising results, this EQC proficiency ring test should be extended to other laboratories and organized twice yearly.

Abstract no.: P01.02

THE DNA BINDING PROTEIN HU FROM *HELICOBACTER PYLORI* PARTICIPATES IN THE STRESS ACID RESPONSE

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The only histone-like protein described in *Helicobacter pylori* is the DNA-binding protein HU. HU binds and bends DNA, which are functions related with protection and integrity of DNA, and regulation of gene expression.
HU is overexpressed in *H. pylori* under acid stress, and that it is downregulated when tested in an acid-sensitive mutant strain (fur), thus suggesting that HU participates in acid stress response mechanisms.
To analyze the role of HU in the acid stress response in vitro now we designed, cloned and purified two substitution mutant proteins, namely HUm2: K3A/S27D and HUm3: K62R/V63N/P64A. Both proteins formed dimers in solution. HUwt binds linear and circular DNA, as pH dependent, and induces compaction of a DNA molecule.
The mutant proteins bind DNA with less affinity than HUwt and HUm3 was unable to induce DNA compaction, thus suggesting that amino acids in positions 62–64 are critical for the bending and compaction functions of HU. DNA protection by HU seems to be related with its DNA-binding ability, because all the three proteins were capable of protecting DNA from both endonucleolytic cleavage and oxidative stress damage.
The *H. pylori* hup negative mutant (hup::cat) has a lower growth rate in pH 7.0 medium compared to the wild type strain, and an acid sensitive phenotype at pH 5.5. Gene expression studies with this hup negative mutant showed that this acid sensitive phenotype can be related to a lack of induction of speA and ureA genes whose products have been involved in acid resistance mechanisms.
FONDECYT 1120126

Abstract no.: P01.03

HELICOBACTER PYLORI AND GASTROESOPHAGEAL MICROBIOTA IN PATIENTS WITH GASTRODUODENAL DISEASES

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Aim: Study on diversity of microbiota and the presence of *Helicobacter pylori* in patients with gastrointestinal tract disorders.
Materials and Methods: In studies were used the biopsy material from 21 patients with chronic gastroduodenitis, gastritis, GERD, gastric ulcer, duodenal ulcer and with other gastrointestinal tract disorders. The mean age of the patients was 47 years. The cultural, biochemical techniques, mass spectrometry (Maldi-ToF, Microflex Bruker optics, Germany) techniques were used.
Results: Using bacteriological method *Helicobacter pylori* was detected in 24% of cases.In gastric and esophageal biopsies diverse microbial population are identified.
Microbial population of the stomach is represented by the following species: Arthrobacter polychromogenes, Arthrobacter scleromae, Streptococcus pneumoniae, Staphylococcus epidermidis, Staph. hominis, Staph. warneri, Streptococcus salivarius, Neisseria flavescens, Bacillus mojavensis, *Helicobacter pylori,* Actinomyces SP., b. licheniformis, Rothia mucilaginosa, Lactobacillus sp., Candida sp.
Among microorganisms-inhabitants of the esophagus found opportunistic bacteria of the genus Neisseria, Rothia mucilaginosa and Gemella. Microaerophilic and aerobic microorganisms with hemolytic activity were found in 48% and 24% cases, respectively.
Conclusions: *Helicobacter pylori* along with accompanying microflora and interacting with it can have an effect on the course, the progression of the disease and the timing of recovery of patients with gatroduodenal tract disorders.
This study will reveal the ratio of different representatives of the microbial community in the stomach, as well as a correlation between the clinical manifestations, the development character of pathogenic processes in patients and the influence of *Helicobacter pylori* contamination on the organism, as well as other pathogenic and opportunistic infections.

Abstract no.: P01.04

SUSCEPTIBILITY OF AMOXICILLIN AND METRONIDAZOLE TO *HELICOBACTER PYLORI* BIOFILM

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The human gastric pathogen *Helicobacter pylori* forms biofilms *in vitro* and *in vivo*. We previously demonstrated that *H. pylori* strain TK1402 biofilm decrease the susceptibility to clarithromycin in vitro. In addition, the expressions of RND family of efflux pumps were significantly increased in biofilm cells. Since the participation of the efflux pumps in the development of multidrug resistance has been reported in *H. pylori*, we examined the effects of biofilm formation on the susceptibility to amoxicillin (AMPC) and metronidazole (MNZ). Minimum inhibitory concentrations (MIC) of strain TK1402 were 0.008 μg/mL and 2 μg/mL to AMPC and MNZ, respectively. Antibiotics susceptibilities of TK1402 mature biofilm to these antibiotics were determined. *H. pylori* biofilm biomass tended to be decreased after treatment with MIC concentration levels of these antibiotics, and after treatment of *H. pylori* with 0.016 μg/mL (2 × MIC) of AMPC or 32 μg/mL (16 × MIC) of MNZ, the biofilm biomass were significantly decreased compared to initial biofilm biomass. Next, we analyzed minimum bactericidal concentrations (MBC) of AMPC or MNZ to biofilm and planktonic cells. The MBC of AMPC or MNZ to biofilm cells were higher (64 μg/mL or 256 μg/mL, respectively) than those to planktonic cells (8 μg/mL or 64 μg/mL, respectively). These results indicated that the biofilm cells were more resistant to these antibiotics than the planktonic cells. Our present results suggest that the assessment of the ability to form biofilms in *H. pylori* is important for eradication of this microorganism.

Abstract no.: P01.05

VARIATION IN SIZE OF *HELICOBACTER PYLORI* CELLS DUE TO ASYMMETRICALLY DIVISION

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Microscopic observations of *Helicobacter pylori* daughter cells showed considerable differences in size and morphology, suggesting that *H. pylori* divides asymmetrically. These differences could be due to *H. pylori* adaptation to human gastric mucus while dividing slowly compared with free living E. coli. It has been proposed that in 50% of the *H. pylori* cells FtsZ rings are localized asymmetrically, thus resulting in different lengths in daughter cells. Twenty gastric biopsies were cultured on selective Brucella agar and incubated at 37°C under microaerophilic conditions. Light microscopic observations were performed as soon as colonies appeared on the plates after three days and continued every day. The size, density, color and concentration of colonies did not influence the microscopic properties of bacterial cells. At fourth day bacterial cells appeared as a mixture of short rods and spirals. Variety of cell forms were seen at the fifth day. Cells showed various short and long spiral, curved and semi-curved shapes, gama forms ( ) and circles. After sixth day cells began to turn into coccoids. Accordingly, high frequency of rods, long and short spirals in fresh culture of *H. pylori* could be due to asymmetrically positioning of FtsZ rings witch is different from other bacteria such as E. coli. Therefore, FtsZ-ring formation and disassembly in *H. pylori* could be responsible for development of short rods and spirals.

Abstract no.: P01.06

ANTIBACTERIAL MECHANISM OF LIPOSOMAL LINOLOENIC ACIDS AGAINST THE MEMBRANE OF *HELICOBACTER PYLORI*

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Background: Although it has been known that fatty acids have antibacterial activity, *in vivo* effects of them remain unclear because of poor solubility and degradation in gastric environment. A liposomal formulation of linolenic acid (LipoLLA), designed for overcoming these challenges, had superior *in vivo* efficacy compared to the standard triple therapy. Therefore, this study investigated the possible antibacterial mechanism of LipoLLA with a focus on the membrane of *H. pylori*.
Methods: Antibacterial activity of liposomal formulation of stearic acid (LipoSA, C18:0), oleic acid (LipoOA, C18:1) and LipoLLA (C18:3) was evaluated using a serial agar dilution method. The permeability of membrane was determined by uptake of the 1-N-phenylnaphthylamin and the release of ATP from cells. Structural changes were analyzed by transmission electron microscopy.
Results: While LipoSA had no effect on *H. pylori*, LipoLLA showed the bactericidal effect with minimal bactericidal concentration (MBC) of <200 ug/mL and this effect occurred within 5 min. Although LipoOA showed inhibition of the bacterial growth, MBC was not detected. LipoLLA and LipoOA permeabilized outer membrane compare to controls and LipoSA ($p < 0.01$). However, the release of ATP was much higher in *H. pylori* treated with LipoLLA than those with LipoOA ($p < 0.01$). Structural changes caused by LipoLLA were seen within 5 min and the main alteration was the detachment of the outer membrane.
Conclusion: The antibacterial effects of liposomal C18 series of fatty acids increased with degree of unsaturation. The bactericidal activity of LipoLLA occurred rapidly and was associated with alteration in the integrity of the bacterial membrane.

Abstract no.: P01.07

EFFECT OF PHENOLIC COMPOUNDS IN *HELICOBACTER PYLORI* PROTEINS STUDIED BY MALDI-TOF

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The objective of this study was to compare the effect of various phenolic compounds in *Helicobacter pylori* proteins. Four phenolic compounds, grape extract (SCOM), grape seed extract (GSE) and 2 resveratrol compounds (R1 and R2) were studied against 2 HP strains. The in vitro activity of the compounds was studied by a disc diffusion method (inhibition zone = IZ). The effect produced by these compounds in HP proteins was carried out by MALDI-TOF. Proteins were extracted by ethanol-formic acid, one microliter applied over a polished steel target plate (Bruker Daltonics), spectra acquired with a Microflex LT mass spectrometer, analyzed with the Bruker Daltonics Biotyper 3.0 software, and a composite correlation index (CCI) matrix created.
CCI indicates the relation between the strains, a lower value indicates less similarity between the same strain under different conditions, so the phenolic compound produces a higher change in HP proteins.

CCI values and the IZ (mm) of 2 compounds

STRAIN	SCOM	GSE
1	0.5573/17	0.5641/18
2	0.8047/23	0.8748/6
3	0.6335/17	0.4310/12

CCI values and the IZ (mm) of 2 compounds

STRAIN	R1	R2
1	0.6148/19	0.6515/21
2	0.8582/18	0.8070/22
3	0.5112/17	0.3823/22

Strain 3 treated with R2 and GSE produced the lower CCI. Strain 1 treated with SCOM and GSE showed the lower CCI. No relationship was found between changes in protein detected by MALDI-TOF and IZ by disc diffusion, indicating that several mechanisms of action must be involved.

Abstract no.: P01.08

PAENIBACILLUS HUMICUS – AN UNEXPECTED COMPONENT OF THE GASTRIC- MICROBIOME?

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Introduction: The impact of other microbiota beyond *H. pylori* of the gastroduodenum attracts renewed interest. The low density of bacteria in the gastroduodenum and the large variability of transient bacteria hampered the

Patient	CLO	Warthin- Starry	Histopathological characteristics	RNA- Analysis	Bacterial diversity
No.1 (57 y)	neg.	no evidence for *H. pylori*	Lymphocytic infiltration in Antrum and Corpus	*H. pylori* detected	Predominant Paenibacillus humicus and Actinomyces sp., less diversity in the observed phylotypes
No.2 (40 y)	neg.	no evidence for *H. pylori*	Patchy neutrophilic infiltrates in Antrum and Corpus	no evidence of *H. pylori*	Predominant Paenibacillus humicus and Actinomyces sp
No.3 (46 y)	neg.	*H. pylori* pos.	Neutrophilic and lymphocytic infiltrates in Antrum and Corpus	*H. pylori* detected	Less diversity in the observed phylotypes

identification of the gastroduodenal microbiome prior to the availability of modern molecular approaches.

Aim: Aim of this pilot study was to analyze the microbiome of the gastroduodenum in three female patients from gastric and duodenal biopsies. Histopathological assessment was performed according to the Syndey System.

Material and Methods: Gastric and duodenal biopsies were obtained from three female patients (40, 46, 57 years). RNA was extracted using the RNeasy Mini Kit and amplicon libraries were generated from extracted RNA. *H. pylori* diagnosis was based on Warthin- Starry- staining and CLO- test.

Results:

Surprisingly, Paenibacilli, a Gram positive aerobic spore, normally found in the environment and so far not identified as pathogen in humans, and Actinomyces sp. were the predominant bacteria in patient 1 and 2. Patients 1 and 3 showed substantially reduced bacterial diversity in RNA analyses.

Conclusion: Application of molecular techniques allows the detection and identification of new bacterial species as part of the gastric microbiota. Presence of *H. pylori* infection appears to reduce bacterial diversity in the stomach. The role of Paenibacillus humicus remains unclear and should be addressed in further studies.

Abstract no.: P01.09

HELICOBACTER PYLORI AND THE ACCOMPANYING MICROBIOTA IN THE INDIAN STOMACH

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Introduction: The microbiota of the Indian stomach and their influence on colonization by *H. pylori* remain largely unknown. We characterized the gastric flora from endoscopic biopsy samples that were positive for the rapid urease test (RUT).

Materials and Methods: Endoscopic biopsy samples were obtained from the gastric pylorus and antrum in 50 patients undergoing endoscopy for indications decided by their physician. Samples that were positive on the bedside RUT were processed further. The molecular tests used involved broad-range PCR and sequencing. Culture was done on Brucella blood agar with modifications in its composition to enhance growth; this was followed by incubation under three conditions (aerobic, anaerobic, microaerophilic) and subsequent identification by MALDI-TOF.

Results: We have amplified the complete 16S rRNA from the samples using universal primers. The amplicons were cloned and sequenced (Sanger method) using vector-specific primers. The predominant organisms identified were *Helicobacter pylori* and *Gamella haemolysans*. Pyrosequencing of the samples is in process.

Discussion: The Indian human stomach harbouring *Helicobacter pylori* is also home to a distinct microbial ecosystem that includes predominantly *Gamella haemolysans*.

Abstract no.: P01.10

COMPARISON OF *H. PYLORI* STATUS IN A PEDIATRIC POPULATION ASSESSED BY QPCR AND RAPID UREA TEST

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The aim of this study was to compare *H. pylori* status by quantitative Polymerase Chain Reaction (qPCR) and rapid urea test (RUT) in a pediatric population from Madrid, Spain.

Gastric biopsies were obtained by upper endoscopy from 52 pediatric patients with gastric symptomatology. RUT was performed using CLO-TEST (Kimberley-Clark) and we identified 20 *H. pylori* positive and 32 *H. pylori* negative specimens in the study. DNA was extracted from antrum gastric biopsies using the UltraClean Tissue & Cells DNA Isolation Kit (MoBio). qPCR was performed using specific 16S *H. pylori* rRNA and universal 16S rRNA qPCR with the LightCycler® 480 Real Time PCR System (Roche).

The log10 DNA copy numbers of *H. pylori* was 3.07 ± 0.35 and 0.60 ± 0.07 for *H. pylori* positive and negative patients respectively ($p < 0.001$). The log10 DNA copy numbers of total bacteria was 3.59 ± 0.25 and 2.60 ± 0.19 in *H. pylori* positive and negative patients respectively ($p = 0.003$). The ratio *H. pylori*/Total bacteria was 1.16 ± 0.37 and 0.06 ± 0.02 in *H. pylori* positive and negative patients respectively ($p < 0.001$)

Our results indicated that *H. pylori* qPCR is a very sensitive method with a great correlation with RUT. As expected, the density of *H. pylori* was significantly higher in *H. pylori* positive patients than in *H. pylori* negative, but also we found that the density of total bacterial was higher in those *H. pylori* positive patients.

Abstract no.: P01.11

HELICOBACTER PYLORI RESTRICTION MODIFICATION SYSTEMS: ROLE BEYOND GENOME PROTECTION

R. Kumar, Y. Prasad and D. N.Rao

Department of Biochemistry, Indian Institute of Science, Bangalore, India

The aim of this study was to compare *H. pylori* status by quantitative Polymerase Chain Reaction (qPCR) and rapid urea test (RUT) in a pediatric population from Madrid, Spain.

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P02 Molecular Genetics and Genomics

Abstract no.: P02.01

ANTI-TUMORIGENIC EFFECT OF PLUMBAGIN BY INDUCTION OF SHP-1 IN HUMAN GASTRIC CARCINOMA CELL LINES

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Background: Plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone) is a plant-drived natural agent extracted from the root of *Plumbago zeylanic*. A recent study reported that plumbagin down-regulated the activity of Janus kinase 2 (JAK2)-signal transducer and activator of transcription 3 (STAT3) pathway to show various anti-tumor effects.

Aim: We aimed in this *in vitro* study to demonstrate the inhibition of JAK2-STAT3 pathway by plumbagin through inducing SH2-containing protein tyrosine phosphatase 1 (SHP-1) expression in gastric cancer cell line.

Methods: We performed Wetern blot to measure SHP-1, phospho-JAK2/STAT3 level, and reverse transcriptase-polymerase chain reaction (RT-PCR) to evaluate target gene expression of STAT3. Several functional studies such as water soluble tetrazolium-1 (WST-1) assay, wound closure assay and matrigel invasion assay were also performed.

Results: Plumbagin induced SHP-1 expression and simultaneously down-regulated phospho-JAK2/STAT3 level via dose-and time-dependant manner in MKN28 cell, a gastric carcinoma cell line which has negative SHP-1 expression. This effect was consistent when JAK2-STAT3 signaling was activated by interleukin-6, and ameliorated when cells were treated with prevanadate, a protein tyrosin phosphatase inhibitor. Furthermore, plumbagin significantly reduced gene expression of cyclin D1, VEGF1, survivin, MMP9, known target products of STAT3 activation in gastric cancinogenesis. The functional effect of plumbagin could be validated as inhibition of cell proliferation, migration and invasion, which are the results of activation of JAK2-STAT3 pathway in gastric cancer cell lines.

Conclusion: Plumbagin is a potential negative regulator of cellular growth, migration and invasion by inhibiting both constitutive and inducible STAT3 activity through induction of SHP-1 in gastric cancer cell line.

Abstract no.: P02.02

EPIGENETIC REGLUATION OF SH2-CONTAINING PROTEIN TYROSINE PHOSPHATASE 1 (SHP1) IN GASTRIC CARCINOMA CELL LINES

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The SH2-containing protein tyrosine phosphatase 1 (SHP1) is an important negative regulator in cytokine mediated signal transduction and cell cycling. Recent studies demonstrated that promoter methylation of SHP1 is frequently observed in gastric adenocarcinoma tissues. We tried in this in vitro study to reveal promoter hypermethylation of SHP1 and to investigate its carcinogenic effects in gastric carcinoma cell lines. We observed that both gene and protein expression of SHP1 were negative in 8 of 10 gastric cancer cell lines (SNU-1, SNU-5, SNU-16, SNU-638, SNU-719, MKN-28, MKN-45, AGS), whereas KATO-III and NCI-N87 showed weakly positive protein expression. Conventional methylation specific PCR (MSP) showed methylation-specific band only in all 10 gastric cancer lines. Bisulfite pyrosequencing revealed 96.5%, 97.3% and 94.8% of methylation frequency in AGS, SNU-719 and MKN-28 cells, respectively, whereas only 5.3% in peripheral blood mononuclear cells. When treating SNU-719, MKN-28 and AGS cells with 5 μmol/L of 5-Aza-2′-deoxycytidine (5-Aza-dc) for 4 days, SHP1 was re-expressed in all three cell lines. When introducing exogenous SHP1 in SNU-719 and MKN-28 cells by transient transfection, protein expression of phospho-JAK2 (Tyr 1007/1008) and phospho-STAT3 (Tyr 705) were substantially down-regulated, which in turn decreased the expression of target genes, including Cyclin D1, MMP-9, VEGF and Survivin. Furthermore, induction of SHP1 significantly reduced cell proliferation and inhibited cell migration and invasion in SNU-719 and MKN-28 cells. In conclusion, epigenetic silencing of SHP1 contributes various carcinogenic effects via JAK2/STAT3 pathway in gastric cancer cell lines.

Abstract no.: P02.03

COMPARATIVE GENOMIC ANALYSIS OF *HELICOBACTER PYLORI* IDENTIFIES THREE DISTINCT LINEAGES

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The host adaptive coevolution of *Helicobacter pylori* with humans led to geographically localized genotypes. A clear understanding of these specific adaptations would prove significant in devising effective interventions. A mixture of people from different ethnic and religious backgrounds in Malaysia provides a better opportunity to understand host adaptation mechanisms and their impact on the genome of *H. pylori*. We sequenced five *H. pylori* isolates and carried out an indepth comparative analysis with 22 other genomes available from Malaysia. The whole genome based phylogenetic tree revealed three major genotypes: hspEastAsia, hspIndia and hpEurope. The presence of *cag*A and *vac*A among core gene clusters explained high pathogenic potential of these strains. Phylogenetic analyses of core clusters identified 311 genes capable of distinguishing EastAsian (Chinese) from non-EastAsian (Indian and Malay) strains, indicating their differential evolution among the two groups. The analysis of outer membrane proteins revealed uniform distribution among the strains. However, each strain harbored ~11 strain specific genes, majority of which were hypothetical with a few encoding putative restriction-modification enzymes. The search for lineage specific factors identified four genes specific to EastAsian lineage of which one was predicted to encode putative lysozyme with others being hypothetical in nature. These and other key lineage specific variations might confer host specific adaptation. Our analysis was important in identification of possible differences among the lineages. Further analysis of these variations together with various genetic and functional studies would allow better understanding of the infection and epidemiology of this gastric pathogen.

Abstract no.: P02.04

INDUCTION STUDY OF *HELICOBACTER PYLORI* B45 PROPHAGE

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Helicobacter pylori B45 prophage was previously UV induced to understand if it could go through a lytic cycle. Electron microscopy revealed a low number of phage particles, which pointed to ineffective induction. The present work aimed to induce the B45 prophage with UV for 0.5, 1, 2 and 5 minutes or with 0.10 μg/mL of ciprofloxacin (1/2 of the MIC). This antibiotic interferes with the DNA replication, which may therefore be a stress factor promoting the prophage induction. Non-induced cultures were incubated under the same conditions as induced ones. After 24 hours of incubation under microaerophilic conditions, DNA was extracted and used in the absolute quantitative real-time PCR. For each induction approach, a single copy gene of *H. pylori* B45 strain (atpA-1) and the prophage integrase gene were quantified, before and after stimuli. This allowed the determination of the number of both *H. pylori* genomes and viral particles present in each sample, using a comparison of the Ct obtained from every DNA quantified with its respective standard curve. An analysis of the results showed that the prophage and bacterial DNAs did not change in the induction process, which suggests the absence of an effective induction. The copy number of prophage genomes was constantly about 1/3 of the copy number of *H. pylori*. Overall, the results suggest that phage particles are present in low copy numbers in the B45 culture and that they cannot be effectively induced by UV or by antibiotic pressure under the present test conditions. Supported by FCT project-PTDC/EBB-EBI/119860/2010.

Abstract no.: P02.05

THE AMPLIFICATION OF GASTRIC CANCER RISK BY CARRYING MULTIPLE FUNCTIONAL SNPS IN INFLAMMATION-ASSOCIATED CYTOKINE GENES

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Background: Intestinal type of gastric cancer (GC) is believed to initiate with *H. pylori*-mediated gastric inflammation. On the other hand, functional single nucleotide polymorphisms (SNPs) in cytokine genes significantly affect recruitment of inflammatory cells into the gastric mucosal lining. Here we have measured the risk enhancing role of single and multiple SNPs in GC.

Methods: In a study comprising of 411 GC and 642 healthy individuals, functional single nucleotide gene polymorphisms (SNPs), namely IL-4-C-590T, IL-6-G-174C, IL-8-T-251A, TNF-α-G-308A, IL-1β T-31C, IL-10 G-1082A and IL-2 G-384T were studied. Unconditional logistic regression model adjusting for age, gender and ethnicity was used to estimate odds ratio and the corresponding 95% confidence intervals.

Results: The most significant GC at risk subjects were carriers of: IL-4-C-590T (OR = 2.94, CI = 1.62–5.33, $p = 0.00001$), IL-6-G-174C (OR = 2.3, CI = 1.22–4.37, $p = 0.010$) and IL-8-T-251A (OR = 2.1, CI = 1.20–3.74, $p = 0.010$). Assessment of multiple SNP carriers revealed that carriers of IL-4-C-590T carriers were at further enhanced risk of GC, if also carried: IL-1β-T-31C (OR = 3.7, CI = 1.47–9.17, $p = 0.005$), IL-6-G-174C (OR = 3.9, CI = 1.54–9.89, $p = 0.004$), IL-8-T-251A (OR = 5.8, CI = 2.19–15.34, $p = 0.0001$), and TNF-α-G-308A (OR=5.7, CI=1.36–23.80, $p = 0.017$). The same occurred for IL-6-G-174C carriers who also carried IL-1β-T-31C (OR=3.21, CI=1.22–8.46, $p = 0.018$), IL-10-G-1082A (OR=5.68, CI=1.19–27.06, $p = 0.029$) and TNF-α-G-308A (OR = 11.24, CI = 1.75–72.13, $p = 0.011$). Carrying TNF-α-G-308A or IL-2-G-384T who also carried IL-8-T-251A were at 3.5 (CI = 1.30–9.45, $p = 0.014$) and 5.1 CI = 1.0–27.96, $p = 0.05$) folds increased risk of GC, respectively.

Conclusion: Single carriers of IL-4-C-590T, IL-6-G-174C, IL-8-T-251A are at approximately 2–3 folds enhanced risk of GC, whereas carrying additional SNPs can further significantly amplify the risk up to more than 11 fold.

Abstract no.: P02.06

GENOMIC FEATURES OF ULCEROGENIC *HELICOBACTER PYLORI* STRAINS ISOLATED FROM CHILDREN

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Whole-genome sequencing (WGS) was used to disclose genomic features of *H. pylori* ulcerogenic strains isolated from children.

Five strains from non-ulcer dyspepsia (NUD) and five strains from peptic ulcer (one gastric ulcer, four duodenal ulcers (DU)) were analyzed by WGS using Illumina technology (MiSeq). Fastq reads were *de novo* assembled using de Bruijn graph method (Velvet V1.2.09). Large indels (LI) associated to ulcerogenic strains, were identified by multiple whole-genome-alignment of the sequenced strains plus *H. pylori* 26695 strain by nucmer3.1.

For now, genome analysis was undertaken for four strains, three NUD and one DU. Genome's length varied from 1.55 Mb-1.63 Mb (GC% ~39), the DU strain displaying the larger genome; all four strains possessed plasmids (sizes from 4194 to 9960 bp).

Five LI were identified: LI1 (3 8228 bp) reflected differences in plasmids content and size; LI2 gave homology to an intact prophage (16 657 bp, 23 CDS, GC% 36.73) present in the DU strain, while one NUD strain possessed two incomplete prophages; LI3 (4659 bp) corresponded to a region with four CDS, present in all but one NUD strain; LI4 (36 169 bp) matched cagPAI, and was present in the DU strain only; LI5 (13 933 bp) displayed homology with 15 CDS, present in the DU strain and in one NUD strain.

LI may be associated with the presence of virulence factors and thus disease development. The strain isolated from the most serious conditions (DU) presented two LI, the well known virulence factor cagPAI and an intact prophage, whose role should be further evaluated.

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Abstract no.: P02.07

GENOME WIDE ASSOCIATION ANALYSES OF *HELICOBACTER PYLORI*

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Helicobacter pylori colonises the gastric mucosa of approximately half the world's population and causes gastritis and peptic ulceration. *H. pylori* infection is the principal pathophysiological step leading to initiation of the inflammatory response and gastric cancer. However, the severity of disease and the ultimate outcome is dependent upon a complex interaction between pathogen and host cell. Chronic inflammation is understood to induce cancer by increasing reactive oxygen and nitrogen species and subsequent DNA damage. This could result from infection with any *H. pylori* stain. However, *H. pylori* populations are highly structured with numerous genotypes existing together in a single patient and these strains can have different disease causing potential. In this work, we have analysed the genome sequences of *H. pylori* (published and unpublished) using Clonal Frame and a Genome Wide Association Study (GWAS) approach. GWAS identifies 30-bp DNA sequences (words) in each genome. This method identifies words that are more strongly associated with a specific phenotype i.e. malignancy than would be expected. In addition, we have performed the micronucleus assay to assess the DNA damage associated with *H. pylori* and AGS cells (gastric adenocarcinoma cell line). Furthermore, we have assessed the motility and growth of these isolates. We present the results of GWAS and phenotypic studies of *H. pylori* associated with malignant and non-malignant gastric pathology. Genetic association study methods, such as these will facilitate the identification of genetic elements likely to cause phenotypes of interest and provide targets for further laboratory investigation.

Abstract no.: P02.08

TOLL-LIKE RECEPTOR 4 WILD TYPE HETEROZYGOSITY OF POLYMORPHISMS +896 AND +1196 IS ASSOCIATED WITH PEPTIC ULCER RISK AND HYPERGASTRINEMIA

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Background: Toll-like receptor 4 (TLR4) is a part of the innate immune system and recognizes lipopolysaccharide from Gram-negative bacteria. We studied the significance of *TLR4* polymorphisms +896 (rs4986790) and +1196 (rs4986791) in the risk of *Helicobacter pylori* related gastroduodenal diseases.

Methods: A case-control study was performed with 87 patients with peptic ulcer, 129 with non-ulcer dyspepsia and 179 controls. *Helicobacter pylori* positivity was assessed by serology and with either bacterial culture or polymerase chain reaction. The relationship of the *TLR4* polymorphisms and *Helicobacter pylori* positivity, endoscopic and histological results and serum concentrations of gastrin-17 and pepsinogens I and II were assessed.

Results: The *TLR4* + 896 and +1196 polymorphisms were in total linkage disequilibrium. The wild type homozygotes had an increased risk for peptic ulcers (OR = 4.390; 95% CI: 1.134–16.998). However, the genotypes did not show any association with *Helicobacter pylori* positivity or the presence or

features of gastric inflammation. Serum gastrin-17 concentration was higher in the wild type homozygotes than in the mutants (median 5.0 pmol/L vs 3.1 pmol/L; $p = 0.001$). Double staining immunohistochemistry of gastric biopsies located TLR4 expression in the G and D cells of antral mucosa.
Conclusions: The *TLR4* + 896/+1196 wild type homozygotes have an increased risk for peptic ulcers compared to the double mutant +896/+1196 genotypes. The association of the risk genotype with high gastrin levels and the expression of TLR4 in G and D cells suggest a role for TLR4 in the regulation of gastric secretion and in the pathogenesis of peptic ulcers.

Abstract no.: P02.09

CYP2C19 GENOTYPES AND FUTURE APPLICATIONS IN PERSONALIZED THERAPIES FOR *HELICOBACTER PYLORI* ERADICATION

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Introduction: Proton Pump Inhibitors (PPIs), have effect in H.pylori eradication by increasing the intragastric pH to 6 or more, improving stability and bioavailability of antibiotics. PPIs are metabolized by CYP2C19 an enzyme encoded by highly polymorphic gene; the genetic polymorphism is classified in three groups: extensive, intermediate and poor metabolizers. Extensive metabolizer genotype is associated with lower eradication rates. Omeprazole, which is one of the PPIs more susceptible to be metabolized by CYP2C19 is often used in Colombia for gastroesophageal reflux (GERD) and for H.pylori eradication therapies usually in doses of 20 mg twice-daily.
Objectives: Determine the distribution of CPY2C19 genetic polymorphisms in patients with H.pylori infection.
Methods: Of 128 patients with *H. pylori* infection were included between 2012 and 2014 at Gastroenterology Center – Clínica Fundadores, Bogotá – Colombia. This study is part of clinical trail "Effect of CYP2C19 in H.pylori eradication". DNA of gastric biopsies was extracted using QIAGEN DNA isolation kit. CYP2C19 genotyping was done by Real Time PCR (Ligthmix kit-Roche).
Results: CYP2C19*1 was the most frequently allele, it was observed in 126/128 (98.4%) of patients. Extensive metabolizators *1/*1; were present in 111/128 (86.7%), intermediate metabolizers *1/*2; in 15/128 (11.7%) and poor metabolizers *2/*2; in 2/128 (1.6%).
Conclusion: Of 86.7% of patients were extensive metabolizers. In order to agree with the results probably is necessary to increase the PPIs doses or to increase the PPIs administration frequency in H.pylori therapies and GERD patients. Finally, CYP2C19 will be use for personalized doses of omeprazole in population.

Abstract no.: P02.10

PROFILE OF MICRORNAS IN GASTRIC CANCER TISSUES AND NORMAL GASTRIC MUCOSA

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Background and Aims: MicroRNAs (miRNAs) are promising biomarkers with diagnostic and prognostic implications. These molecules are a group of small non-coding RNAs that modulate gene expression. MiRNA are deregulated in different tumors including gastric cancer (GC). The data on deregulated microRNA profile in GC tissues mandates further research.
Aims & Methods: The aim of our study was to evaluate and compare miRNA profile in GC tissue and normal gastric mucosa from healthy individuals. MiRNAs from fresh frozen tissues were profiled using Applied Biosystems ® ViiA™ 7 RT-PCR system with TaqMan® Array Micro Fluidic A Cards in 15 tissue samples of primary GC and 11 normal gastric tissues from healthy controls. Log2-fold change (log2FC) calculations were performed using GenEx software.
Results: The results of microRNA profiling revealed 3 down-regulated miRNAs in GC tissue samples compared to normal gastric tissue: hsa-miR-135a (log2FC = −7.96199, $p = 1.73E-06$), hsa-miR-26b (log2FC = −2.2343, $p = 1.2E-05$), hsa-miR-148a (log2FC = −6.73728, $p = 2.13E-05$). The analysis also revealed 15 significantly up-regulated miRNAs in GC tissues compared to normal gastric mucosa: hsa-miR-214 3 (log2FC = 7.6098, $p = 2.32E-06$), hsa-miR-155 (log2FC = 5.53734, $p = 2.17E-05$), hsa-miR-146b (log2FC = 4.59012, $p = 3.17E-05$), hsa-miR-345 (log2FC = 2.21088, $p = 3.56E-05$), hsa-miR-223 (log2FC = 6.21766, $p = 5.53E-05$), hsa-miR-126 (log2FC = 2.36791, $p = 8.32E-05$), hsa-miR-345 (log2FC = 2.21088, $p = 3.56E-05$), hsa-miR-223 (log2FC = 6.21766, $p = 5.53E-05$), hsa-miR-126 (log2FC = 2.36791, $p = 8.32E-05$), hsa-miR-484 (log2FC = 3.02072, $p = 0.000116$), hsa-miR-140-3p (log2FC = 2.55172, $p = 0.000123$), hsa-miR-10a (log2FC = 2.11934, $p = 0.000194$), hsa-miR-16 (log2FC = 2.1092, $p = 0.0002$), hsa-miR-24 (log2FC = 2.48963, $p = 0.000221$), hsa-miR-331 (log2FC = 2.58057, $p = 0.000224$).
Conclusions: MicroRNA profiling analysis revealed three differentially down-regulated and 15 up-regualted miRNAs in GC tissue compared to normal gastric mucosa. This profile may serve as potential biomarker for GC and needs validation in further studies.

Abstract no.: P02.11

SERUM MIRNA-21 EXPRESSION IN GASTRIC CANCER PATIENTS AS A SCREENING BIOMARKER

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Background: MicroRNAs (miRNAs) expression is deregulated in *Helicobacter pylori*-infected gastric mucosa and gastric cancer tissue. Recent studies have demonstrated that these non-coding small RNA molecules are also released into the circulation and can reflect the presence of tumors. The aim of this study was to investigate serum miR-21 levels in patients with gastric cancer (GC) and assess its potential diagnostic and prognostic values.
Methods: Serum samples were collected from 30 gastric cancer patients (mean age ± standard deviation, 58.6 ± 14.2 years) and 25 cancer-free endoscopy controls (56 ± 13.3 years). The expression of miR-21 in serum samples was determined by real-time reverse transcriptase-quantitative polymerase chain reaction (RT-qPCR), using miR-16 as the internal refer¬ence gene. Comparison between normalized gene expression level in the study groups was performed using Relative Expression Software Tool software (REST© 2009, Qiagen).
Results: Using miR-16 as an endogenous control, serum expression of miR-21 in our GC cases, in comparison to controls, was markedly up-regulated by a mean factor of 5.56 fold ($p = 0.000$). Sub-stratification of gastric cancer according to tumor stage identified a stepwise increase of miR-21 expression by 3.90 and 5.94 folds for early (I&II, $p = 0.037$) and late (III&IV, $p = 0.001$) stages, respectively.
Conclusion: In accordance with the tumorigenic role of miR-21, our results provide further evidence that serum miR-21 can be used as a screening biomarker for diagnosis and monitoring of gastric cancer progression. Serum profiling of larger number of cases and controls will validate these findings.

Abstract no.: P02.12

MANNOSE-BINDING LECTIN 2 POLYMORPHISMS AT CODON 52, 54 AND 57 DO NOT INCREASE THE PREVALENCE OF *HELICOBACTER PYLORI* INFECTION AND THE RISK OF GASTRODUODENAL DISEASES IN KOREAN POPULATION

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Background/Aims: Mannose-binding lectin 2 (MBL2) is an important constituent of the innate immune system. Some studies of possible association of *MBL2* haplotype and the susceptibility of *Helicobacter pylori* infection as well as the risk of gastric cancer (GC) were reported. We examined whether polymorphisms of *MBL2* codon 52, 54, and 57 influence the prevalence of *H. pylori* infection and *H. pylori*-related gastroduodenal disease in Korean population.
Material & Methods: Of 177 *H. pylori*-negative control group, 186 patients with *H. pylori*-positive chronic gastritis, 222 GC and 173 duodenal ulcer (DU) patients were included in this study. Polymorphisms of *MBL2* at codon 52, 54, and 57 were examined by PCR-RFLP. Serum MBL concentration as the functional activity of MBL2 protein, was measured by ELISA.

Results: In Korean population, polymorphic variants at codon 52 and 57 were not found, but only found at codon 54. Polymorphism of *MBL2* codon 54 G/A does not increase the prevalence of *H. pylori* infection as well as the risk of GC or DU. Serum MBL concentration was significantly different according to *MBL2* codon 54 G/G (wild type, 1731 ± 335.5 ng/mL), G/A (heterozygote, 166.6 ± 45.9 ng/mL), and A/A genotype (mutant type, 4.8 ± 5.8 ng/mL). However, serum MBL concentration was not different among the gastroduodenal disease groups.
Conclusions: Polymorphisms of *MBL2* codon 52, 54, and 57 were not associated with *H. pylori* infection prevalence and the risk of GC or DU. The functional activity of MBL2 was significantly different according to its *MBL2* codon 54 genotype.

Abstract no.: P02.13

THE RELATIONSHIP OF CAGA EPIYA MOTIF POLYMORPHISM AND H.PYLORI RELATED DISEASE OUTCOMES IN CHINA

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Background: To find out the relationship between CagA EPIYA motif polymorphism and *H.pylori* related disease outcomes.
Methods: PCR was performed on 170 clinical H .pylori strains from the first affiliated hospital of Nanchang university to study the polymorphism of CagA EPIYA motif.
Results: For 170 clinical H.pylori strains, 100% of them have cagA gene. There were 0–4 EPIYA motifs in them, and 4 strains contained 4 EPIYA motifs, including two strains of gastric cancer, and 2 strains containing 2 EPIYA motifs were all chronic gastritis strains. 161 strains containing 3 EPIYA motifs and 3 strains without EPIYA motifs were no significant correlation with diseases. All H.pylori isolates can be divided into 3 sequence types, including AB type (2EPIYA motifs), ABD type (3 EPIYA motifs) and AABD type (4 EPIYA motifs), all of which are oriental type (TIDD). In this study, all strains were identified as TIDD.
We further analyzed EPIYA motif polymorphisms and found 2 strains with EPIYA-A mutation were from chronic gastritis. 2/9 strains with EPIYA-B mutations were from gastric cancer, and 7/9 were from duodenal ulcer. These results demonstrated that the EPIYA-B mutated strains had stronger virulence.
Conclusion: 1. CagA gene positive rate in our study was 100% which was significantly higher than other western countries, and all the cagA gene types are East Asian type.
2. *H.pylori* pathogenicity enhanced with the number of CagA EPIYA motifs. And the virulence of strains with EPIYA-B mutation was stronger than strains with EPIYA-A mutantion and non-mutantion.

Abstract no.: P02.14

EVALUATION OF C421A POLYMORPHISM AND EXPRESSION OF ABCG2 GENE IN THE GROUP OF PATIENTS WITH GASTRIC ADENOCARCINOMA

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Gastric cancer is one of the most common malignant diseases.The pathogenesis of gastric cancer development is not entirely known. As a risk factors to development of this diseases are mentioned: dietary habits, chronic inflammation and *Helicobacter pylori* infection. Nowadays also genetic factors as increased predisposition to gastric cancer development are taken into consideration.ABCG2 gene encodes protein BCRP which is located in many normal tissue including digestive tract. BCRP through efflux of xenobiotics from cells into extracellular environment plays a protective role. ABCG2 gene is polymorphic, one of the most common SNP of this gene is C421A. It leads to substitution C on A which is associated with amino acid exchange in the BCRP structure. Polymorphism at position C421A may reduce activity of protein. As a result it may leads to accumulation of potentially carcinogenic xenobiotics in cells and increase the risk of gastric cancer development.
Aim of the study was genotyping at position C421A and evaluation of ABCG2 gene expression in tissue specimen of gastric cancer from patients with gastric adenocarcinoma and comparison the frequency of obtained genotypes distribution with control group.
Investigated group (N = 19): tissue specimen of gastric cancer: Control group (N = 65): blood taken from blood donors.
Methods: RFLP, qualitative and quantitative PCR.
In all samples of control group and samples of investigated group the CC genotype for SNP 421 was found. So far in all samples of investigated group ABCBG2 qualitatively gene expression were demonstrated.

Abstract no.: P02.15

A STUDY OF *HELICOBACTER PYLORI* OUTER-MEMBRANE (HOM) PROTEIN B POLYMORPHISM IN CHINA

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Background: Detecting homA and homB gene, to determine whether the homA and homB associated with clinical outcome of *H. pylori* infection, especially with gastric cancer.
Methods: PCR was performed on 170 clinical H .pylori strains from the first affiliated hospital of Nanchang university to study the presence of the homA and homB.
Results: 1 The distribution of homA and homB in clinical diseases

	Single homA(+)	Single homB(+)	homA and homB(+)
CG	10.4% (5/48)	68.8% (33/48)	20.8% (10/48)
CU	13.3% (10/75)	68.0% (51/75)	18.7% (14/75)
GU	20.0% (4/20)	75.0% (15/20)	5.0% (1/20)
GC	22.2% (6/27)	74.1% (20/27)	3.7% (1/27)*
chi square	$X^2 = 2.480$	$X^2 = 0.630$	$X^2 = 6.231$
p value	$p = 0.479$	$p = 0.890$	$p = 0.101$

*Note: Is vs CG $p < 0.05$

2. After optimizing PCR and sequencing conditions, 59 full-length sequences were obtained ultimately from 145 homB gene positive strains. Among them, the sequencing success rate of gastric cancer (9.5%) was significantly lower than the other three groups (50.0%~66.7%) ($p < 0.05$).
Conclusion: 1. HomA gene positive rate of H.pylori from China was lower than homB gene, and homB positive rate was much higher than that of Western countries.
2. HomA and homB single positive rate was no significant difference within different diseases, but homA and homB double positive rate in gastric cancer strains was significantly lower than that in chronic gastritis strains. Furthermore, sequencing failure proportion of homB from gastric cancer strains was significantly higher than other three kinds of diseases, suggesting homB gene of gastric cancer strains may occupied complex senior structure and multi-repetitive sequences.

Abstract no.: P02.16

TYPING OF *HELICOBACTER PYLORI* 3′ END MOTIFS OF CAGA FROM PATIENTS WITH GASTRITIS AND PEPTIC ULCER DISEASES

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CagA protein is one of the most important *H.pylori* virulence factors that have been introduced. After exposure of *H.pylori* cagA + strains to epithelial cells, CagA injected directly into the host gastric epithelial cells where undergoes tyrosine phosphorylation at the 3′carboxyl-terminal end (EPIYA) motifs. The phosphorylated CagA disrupts cell signaling pathways and induces alterations in epithelial cell activity and morphology. The biological activity of CagA is determined by variation in the tyrosine phosphorylation motif sites. In this case there are four distinct EPIYA segments, EPIYA-A, EPIYA-B, EPIYA-C and EPIYA-D. In this study, we assessed the diversity and the type of the CagA EPIYA motifs of H.pylori strains isolated from Iranian patients and investigation their association with gastritis, gastric ulcer and duodenal ulcer. Biopsies that were taken from patient's endoscopy were cultured on selective Brucella agar supplemented with defibrinated sheep blood. To determine the CagA EPIYA motifs, PCR, sequencing and alignment with Bioinformatic analysis were performed. From 168 H.pylori cagA+ strains 158(93.5%) ABC, 9(5.4%) ABCCC and only

one mixed types of ABC+ABCCC and one ABCC were detected. There was no EPIYA- D segment. ABC (158, 93.5%) was the most frequent motifs in all disease groups but ABCCC (16%) was more frequent in gastric ulcer group than in others. Data have been shown that CagA from Iranian H.pylori strains are western type and all strains have active phosphorylation sites and there is an association between C segments repeats and gastric ulcer in Iranian patients that were studied.

Abstract no.: P02.17

PREVALENCE OF *HELICOBACTER PYLORI* GENOTYPES IN ITALIAN PATIENTS

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Helicobacter pylori is known to play a role in the pathogeneses of chronic gastritis, peptic ulcer disease, gastric cancer and gastric Mucosa-Associated Lymphoid Tissue (MALT) lymphoma. Genes, such as vacA, cagA, cagE, iceA and babA, may play important roles in the pathogenesis of *H. pylori* infection.
The vacuolating cytotoxin gene (vacA) is present in all *H. pylori* strains, but, since its known to be differentially expressed, vacA subtypes can be determined.
The cytotoxin associated gene A (cagA) positive strains induce interleukin-8 (IL-8) production and mucosal inflammation, while cagE has also been associated with a more severe clinical outcome.
The induced by contact with epithelium (iceA) gene has two allelic variants: iceA1 and iceA2. The Allelic variant iceA1 is associated with peptic ulcer disease.
For blood group antigen-binding adhesin gene (babA) three alleles have been identified (babA1, babA2, babB), but only the babA2 appears to be related to peptic ulcers and gastric cancer.
We analyzed 86 *H. pylori* strains obtained from gastric biopsies of 86 Italian patients respectively 65 female and 21 male.
Genotypes detected were: vacA 86/86 (100%), cagA 40/86 (46.5%), cagE 40/86 (46.5%), iceA1 27/86(31.4%), iceA2 25/86 (29%) and babA2 78/86 (90.1%).
Genotypes detection could be used to monitor in a targeted manner the evolution of the infection-positive patients.
Further larger scale researches are necessary in order to assess the possible role of cag A and other virulence genes in different clinical outcomes which is correlated with *H. pylori* infections.

Abstract no.: P02.18

ESTABLISHMENT OF AN IN VITRO INFECTION MODEL OF *H. PYLORI* USING HUMAN PRIMARY GASTRIC EPITHELIAL CELLS

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Recent advancement in stem cell and tissue culture has made possible to cultivate primary epithelial cells from different tissue without their mesenchimal niche. This pure long-term living tissue is growing in 3D structures and are commonly called organoids. We have recently establish a protocol for the cultivation of human gastric organoids. Spherical 3D structure (spheroids) are growing within a specific extracellular matrix (Matrigel) in a media supplemented with a specific cocktail of morphogens, growth factor, and inhibitors. Withdrawal of the morphogens from the medium results in differentiation of spheroids into organoids with a more complex and folded structure. Spheroids and organoids can be used as a source of cells to culture in a 2D format, forming a semi-organized planar culture of polarized cells, suitable for the infection with H. pylori. This infection model is particularly appropriate to study the early molecular events, which are specifically triggered by the pathogen, involved in the onset of cancer. Preliminary experiments suggest that H. pylori induces vacualization and elongation (hummingbird phenotype) of the infected cells. CagA is translocated and phosphorylated in the host cells. Inflammation related genes are modulated. Both cells and pathogens partially survive during short infection periods and current experimental efforts are directed toward establishing a long lasting infection. Analysis of gene expression and DNA damage induced mutations are going to be performed at different time points in order to understand any specific role of the pathogen in intestinal metaplasia and gastric cancer.
*Equal contribution

P03 Virulence Factors and Pathogenesis

Abstract no.: P03.01

NNUCLEAR-TRANSLOCATED LRP1-ICD IS RELATED TO THE FORMATION OF AUTOPHAGOLYSOSOME ASSOCIATED WITH CAGA DEGRADATION IN GASTRIC EPITHELIAL CELLS INFECTED WITH *H. PYLORI* VIA INDUCTION OF LAMP1 EXPRESSIONS

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Objective: *Helicobacter pylori* effector protein CagA acts as an oncoprotein. Recently, we observed that translocated CagA was degraded by autophagy (Cell Host & Microbe, 2012). The autophagy was activated by VacA via binding to low-density lipoprotein receptor-related protein-1 (LRP1). LRP1 is regulated by proteolytic processing, and then LRP1-intracellular domain (LRP1-ICD) is translocated to nucleus. Although it is known that LRP1 have the ability to bind ligand to several signal transduction pathways, the role of the autophagy induction through LRP1 has remained unclear. The present study was conducted to examine LRP1-signal transduction to the autophagy.

Methods: Autophagy was assessed by autophagic flux assay. The participation of LRP1-ICD in autophagy was assessed using an lrp1-siRNA, and the localization was assessed by western blot following subcellular fractionation and immunocytochemistry. LAMP1 expression systems were analyzed by Chip assays.

Results: Nuclear translocation of LRP1-ICD was enhanced in AGS cells at 24 hours after *H. pylori* infection (during the autophagy induction). Expressions of Lamp1 were significantly increased during autophagy induction. Lamp1 expressions were repressed by lrp1-siRNA, and the direct binding of LRP1-ICD to LAMP1 promoter was enhanced during autophagy induction, suggesting that Lamp1 expressions were regulated by nuclear-translocated LRP1-ICD. Lamp1 colocalized with both autophagosomes and autophagolysosomes induced by *H. pylori*. The specific lamp1-knockdown repressed the formation of autophagolysosome, leading to the accumulation of intracellular CagA.

Conclusion: Nuclear-translocated LRP1-ICD enhanced LAMP1 expressions and enhanced the fusion between autophagosomes and Lamp1-positive lysosomes, leading to CagA degradation.

Abstract no.: P03.02

COMPARATIVE GENOMICS OF GASTRIC *HELICOBACTER* SPECIES: ANALYSIS OF THE OUTER MEMBRANE PROTEINS

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Various non-*H. pylori Helicobacter* (NHPH) species have been identified as colonising the gastric mucosa of mammals. Several of these NHPH have a pathogenic potential in different animal hosts, including humans. Adherence to the gastric mucosa is widely assumed to play a critical role in the initial colonization and persistence of *Helicobacter* in the stomach. *H. pylori* is equipped with a large number of outer membrane proteins (OMPs), and their role in the adhesion process has been well-studied. Recent adherence assays have shown that several NHPH are able to bind to the gastric mucosa and we hypothesise that OMPs are central to this binding phenotype. In this study, the genome sequences of a variety of *H. pylori* and 11 different NHPH were analysed to identify the OMPs using the HHOMP tool and BLASTP, which compares the genome data to an OMP database. To determine the phylogenetic relationships, OMPs were aligned with the known *H. pylori* OMPs. While most OMPs were shared by all gastric *Helicobacter* species, some were species-specific. Interestingly, the feline and canine gastric *Helicobacter* species and *H. suis*, all lack the typical *H. pylori* adhesins characterised previously. On the other hand, these NHPH contain an operon consisting of 6 hof genes (*hofA/F/E/G/C/D*), which is absent from the *H. pylori, H. acinonychis* and *H. cetorum* genomes. The role of the proteins encoded by this operon in adhering to the gastric mucosa was further investigated. Results obtained indicate that HofF, HofE and HofG OMPs are putative adhesins.

Abstract no.: P03.03

TRANSCRIPTIONAL RESPONSES OF *HELICOBACTER PYLORI* TO SUBINHIBITORY CONCENTRATIONS OF HUMAN β-DEFENSIN 3

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Secretion of human β-defensin (hβD)-3 by gastric epithelial cells contributes to effective surveillance against microbial populations in proximity to the gastric mucus. However, persistence of *H. pylori* (Hp) in the gastric mucosa remains a puzzling aspect of the host – microbe interaction leading to consideration that escape or suppression of innate immunity mechanisms, including hβDs, counts towards Hp enhanced survival in the gastric environment.

In this study, the responses of Hp-J99 strain to subinhibitory concentrations of hβD3 were investigated using Hp-specific microarrays. Significant changes in the transcriptional profiles of Hp-strain tested demonstrated by the induction or suppression of multiple gene components of distinct regulatory mechanisms and/or signaling pathways similar to those activated by stress responses. These changes included: i. modification of the cell wall stimulon as means to prevent hβD binding, activation of transmembrane efflux pumps and maintainance of osmotic balance on both sides of the outer membrane; ii. activation of DNA repair mechanisms, thereby promoting genetic recombination; iii. profound induction of genes encoding factors related to chemotaxis and flagellar apparatus; iv. activation of defense mechanisms, directly linked to Hp virulence, against oxidative stress; v. increased, apo-fur-dependent production of urease; and vi. suppression of RNA replication, expression of ribosomal proteins and enzymes necessary for amino acid metabolism, possibly reflecting the selective reduction of metabolic functions and cell proliferation.

In conclusion, this study illustrates conserved and novel mechanisms of bacterial resistance to hβDs and provides a starting point for detailed analyses of numerous genes involved in adaptation to the gastric environment.

Abstract no.: P03.04

HELICOBACTER PYLORI CAGA PROMOTES SNAIL-MEDIATED EPITHELIAL MESENCHYMAL TRANSITION BY REDUCING GSK-3 ACTIVITY

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Bona fide oncoproteincytotoxin associated gene A (CagA), a major virulence factor of *H. pylori*, is delivered into gastric epithelial cells via a type IV secretion, resulting in cellular transformation.The loss of epithelial adhesion accompanied by the epithelial mesenchymal transition (EMT) is a well-known genetic background of gastric cancer. Although causality of CagA on gastric cancer is evident, the link between CagA and EMT has not been identified. Here we show that the CagA induces EMT by stabilizing Snail, a zinc-finger protein of E-cadherin repressor. Mechanistically, the CagA binds to the GSK-3 similar to Axin, leading to a shift of the GSK-3 to an insoluble fraction and resulting in reduced GSK-3 activity. Furthermore, Snail protein abundanceis increased in *H. pylori* infected epithelium on clinical tissues. These results suggest that *H. pylori* CagA acts as a pathogenic scaffold protein inducing Snail-mediated EMT via the depletion of GSK-3.

Abstract no.: P03.05

H. PYLORI γ-GLUTAMYLTRANSPEPTIDASE TOLERIZES HUMAN DENDRITIC CELLS VIA GLUTAMATE RECEPTOR SIGNALING

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Despite of eliciting a strong inflammatory response, *Helicobacter pylori* (*H. pylori*) has developed several mechanisms to evade the host's immune system. Importantly, the virulence factor γ-glutamyltranspeptidase (gGT) has been linked to tolerance by shaping the innate immune response to a tolerogenic phenotype in mice. However, the molecular mechanisms involved remain mostly unknown. In the present study, we show that *H. pylori* gGT tolerizes human dendritic cells, independently of their maturation status, to drive a regulatory T cell response. Due to its enzymatic activity, gGT converts glutamine into glutamate, which prevents the production of the pro-inflammatory cytokine IL-6, thereby favoring the development of regulatory T cells over Th1 and Th17 cells during *H. pylori* infection. These effects seem to be mediated by PKA signaling, and contribute to *H. pylori* persistence in the gastric mucosa.

Abstract no.: P03.06

IMMUNOLOGIC RESPONSE TO *H. PYLORI* CAGA IS STRONGLY DEPENDENT ON *VACA* POLYMORPHISM

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Background: Serological response to *H.pylori* CagA protein is widely used as a surrogate biomarker for *cagA*, however, exact biological relationship between *H.pylori* strains and serological response is still not clear. Here, we prospectively investigate *H.pylori* strains with regard to *cagA* and *vacA* and investigate its dependent CagA serologic host response.
Methods: From total 331 patients prospectively recruited, as part of HELDIV-PAT/ERA-NET, *H.pylori* microbiological cultivation was successful in 86 patients (chronic gastritis, atrophic gastritis, peptic ulcer diseases and gastric cancer) at least in one of the biopsies from corpus and/or antrum. *H.pylori cagA*, EPIYA and *vacA* s/m status as well as *cagA* and *glmM* mRNA were determined by PCR. Anti-CagA IgG status was evaluated using commercially available ELISA.
Results: Of 150 *H. pylori* isolates were successful cultivated from 86 patients. 81 (94.2%) of them were *H.pylori cagA* positive, however, only 27 (31.4%) showed serological response to CagA. CagA mRNA expression was negative in 21 (25.9%) of *cagA* strains, suggesting translation defect as partial mechanism. VacA polymorphism but not EPIYA motifs were significantly associated with CagA IgG response of the host to *H.pylori* infection with *cagA* strain. Despite relatively similar distribution among *vacA* genotypes, 20 of 36 *H.pylori cagA*+ (55.6%) patients with *vacA* s1 m1, 7 of 19 (36.8%) were positive for anti-CagA IgG. None of the patients with *vacA* s2 m2 *H.pylori* strains showed serological host response to CagA.
Conclusions: Serological response to *H.pylori cagA*+ strains is strongly dependent on *vacA* polymorphism, while CagA IgG has only low predictive value as surrogate biomarker for *cagA*.

Abstract no.: P03.07

H.PYLORI CAGA$^+$, *VACAS1 M2* $^+$, AND *HPAA*$^+$ STRAINS PROMOTES T-HELPER 17 RESPONSE INSTEAD OF T HELPER 1 THAT LEADS TO INTESTINAL METAPLASIA IN TURKISH *H. PYLORI*-INFECTED GASTRITIS AND ULCER PATIENTS

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Helicobacter pylori (H.pylori) can cause gastric malignancies such as gastritis and ulcer. *H.pylori*-induced diseases can be associated with bacteria's virulence factors, host genetic factors and immune response. Virulence factors with potential value for specific pathologies are the *cag A, vacA, oipA, babA,* n*apA, dupA* and *hpaA. H.pylori* infection induces T helper 1 (Th1) & T helper 17 (Th17) driven immune response in infected patients. This study aims to correlate *H.pylori*-induced gastric malignancies with *H.pylori* virulence factors and T helper response. In total, 80 Turkish *H. pylori*-infected gastritis and ulcer patients were enrolled to the study. All samples were tested for various *H.pylori* virulence factors using multiplex-PCR. Also, Th1 (IFN-) and Th17 (IL-17) specific cytokine mRNA expression levels were measured using real-time-PCR. The majority of *H.pylori* strains that infects ulcer and gastritis patients, are positive for *hpaA* and *vacA s1, m2* but negative for *oipA, babA, napA,* and *dupA*. Also, the vast majority of the *H.pylori* strains isolated from gastritis patients were positive for *cagA*. However, *H.pylori* strains that induce ulcer were *cagA* negative. All *H.pylori* strains isolated from ulcer and gastritis patients with intestinal metaplasia are positive for *vacA s1/m2* genotype and majority are positive for *hpaA*. Additionally, *H.pylori* infected ulcer and gastritis patients are showing mainly a Th17 response instead of Th1 response. Overall our data suggests that patients infected with *H.pylori* strains positive for *cagA, vacAs1 m2,* and *HpaA* are at higher risk for developing Th17- driven intestinal metaplasia.

Abstract no.: P03.08

ROLE OF BACTERIAL OUTER MEMBRANE PROTEINS IN PATHOGENESIS OF *HELICOBACTER PYLORI*: AN INSIGHT INTO VARIOUS ASPECTS OF *H. PYLORI* INFECTION

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Aim: To study gene expression of bacterial OMPs and *cagA* in patients with *H. pylori* infection by RT RT-PCR and evaluate the reliability of the test.
Methods: On the basis of positive rapid urease test (RUT),culture and histopathology,biopsies of 97 patients with gastritis were included.The antrum and corpus biopsies of 58 patients were used together for RNA extraction while 39 patients were processed separately.The expression of 5 target and 2 house-keeping genes were determined by RT RT-PCR.The threshold cycle (Ct)and normalized ΔCt were obtained.
Results: RUT, culture and histopatology positive results of 116 patients were 76/116(66%),44/100(44%),43/64(67%) for antrum and 22/62(35%),29/95 (31%),38/56(68%) for corpus respectively.Of the 97 patients (43 male,54 female;mean age 50.43 ± 14.48) 76 patients (46/58 and 30/39) were positive for *H. pylori* by PCR.Gene expression frequencies of *cagA,omp6,omp13,omp18* and *omp20* in the antrum and corpus together of 46 PCR+ patients were 30(65%),35 (76%),35(76%),46(100%) and 36(78%) respectively.While in separately processed the antrum and corpus of 30 PCR+ patients were 16(53%),21(70%),24 (80%),29(97%),23(77%)for antrum and 15(50%),18(60%),25(83%),28(93%), 24(80%) for corpus respectively.The ΔCt's of *cagA* and *omp13* were significantly higher in the corpus of patients with pan-gastritis than in patients with antral gastritis ($p = 0.014$, $p = 0.011$).Gene expression frequency of *omp20* was significantly higher in the corpus of patients with erythema than in patients without erythema ($p = 0.02$).The expression of *cagA,omp6,omp13* and *omp18* was detected in *H. pylori* NCTC 11637 which confirmed the results of gene expression in patients.RT RT-PCR showed good precision with no cross reaction.
Conclusion: This study revealed that expression of *cagA,omp13* and *omp20* genes were associated with clinical findings.RT RT-PCR was found a convenient and reliable method.

Abstract no.: P03.09

RELEVANCE OF 3-END REGION POLYMORPHISMS OF *HELICOBACTER PYLORI VACA* GENE TO GASTRODUODENAL DISEASES

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Significance of the 3 -end region polymorphisms (denoted *c1/c2-c2*: no deletion) of *Helicobacter pylori vacA* gene in determining risk of gastroduodenal diseases has still not been understood. The aim was to determine the role of *vacA*

c-region in relation to peptic ulcer disease (PUD) risk. We assessed the *vacA s-, m-, i-, d-,* and *c*-region genotypes and *cagA* status in 171 *H. pylori* isolates recovered from different regions of Iran by PCR. The subjects included 114/171 with non-atrophic gastritis (NAG), and 57/171 with PUD. The frequency of *vacA s1* was 92.4%, *vacA s2* 8.8%, *m1* 26.3%, *m2* 73.7%, *i1* 43.3%, *i2* 57.3%, *d1* 40.9%, *d2* 59.1%, *c1* 23.4%, *c2* 79.5%, and *cagA* 67.8%. Statistical analysis showed that frequency of the *vacA i1, cagA, vacA m2i1, vacA i1d1, vacA i1c2, vacA i1/cagA,* and *vacA c2/cagA* genotypes in patients with PUD (58.6%, 81.0%, 29.8%, 43.9%, 40.4%, 49.1%, and 61.4%, respectively) was higher than in those with NAG (35.4%, 61.1%, 14.0%, 28.1%, 14.3%, 30.7%, and 42.1%, respectively) ($p < 0.05$). There was a lower prevalence of the *vacA m2i2, vacA i2d2,* and *vacA i2c2* genotypes in patients with PUD (38.6%, 35.1%, and 38.6%, respectively), compared with in those with NAG group (63.2%, 57.0%, and 61.4%, respectively) ($p < 0.05$). The *vacA s-, m-, d-,* and *c*-region genotypes were not independently associated to PUD risk. We have proposed that the *H. pylori vacA i1, cagA, vacA m2i1, vacA i1d1, vacA i1c2, vacA i1/cagA,* and *vacA c2/cagA* genotypes could be improved predictor of risk of PUD in Iran.

Abstract no.: P03.10

VIRULENCE MARKERS OF *H. PYLORI* AND TNF-ALPHA POLYMORPHISM (G-308A) IN BRAZILIAN PATIENTS

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Tumor Necrosis Factor-Alpha (TNF-α), is a multifunctional pro-inflammatory cytokine. Several studies demonstrated that TNF-α acts as a potent inhibitor of gastric secretion after *Helicobacter pylori* infection, contributing to the development of gastric diseases. The present study characterized the -308 (rs1800629) polymorphism of TNF-α by PCR-RFLP and verified the presence of *dupA, cagA* and *vacA* genes. Furthermore, we evaluated the association among virulence factors, genotypes and histological findings. Gastric biopsies were obtained from 425 dyspeptic patients and 36 with gastric cancer (GC), however, of each patient with GC, were collected two biopsies, one from the neoplastic tissue and other from non-neoplastic region, totalizing 72 samples. *H. pylori* was detected in 218/425 dyspeptic patients and 27/36 patients with GC. In relation the dyspeptic patients, we verified a significant association between *dupA* and *cagA* gene and between s1/m1 and *dupA* gene (Table 1). In relation to the gastric cancer samples, no association among virulence markers was verified but *dupA* gene was more prevalent in non-neoplastic tissue suggesting a reduced risk for GC. The genotype distributions of TNF-a G-308A showed no relationship between the histological groups and no differences in relation to the presence of *H. pylori* infection.

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Table 1 Frequency of genes cagA, dupA and vacA in *H. pylori* strains isolated from 218 patients

Virulence Markers	*vacA*							
	dupA+	*dupA-*	Total	*s1/m1*	*s2/m2*	*s1/m2*	Other	Total
cagA+	60*	45	*105*	81*	9	8	7	*105*
cagA -	35	78	*113*	26	76	7	4	*113*
Total	*95*	*123*	*218*	*107*	*85*	*15*	*11*	*218*
dupA +				61*	25	7	2	*95*
dupA -				46	60	8	9	*123*
Total				*107*	*85*	*15*	*11*	*218*

*p statistically significant.

Abstract no.: P03.11

HELICOBACTER PYLORI OR EPSTEIN-BARR VIRUS (EBV) INFECTION AND TP53 OR BCL-2 PROTEIN EXPRESSION IN GASTRIC CARCINOMAS

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Background: In etiopathogenesis of gastric carcinoma (GC) a significant role of infection not only by H.pylori, but also Epstein-Barr virus (EBV) has already been documented. Crucial role in the carcinogenesis process is played with TP53 protein and Bcl-2 gene protein. It remains unclear whether in GC p53-abnormalities and Bcl-2 expression are dependent on presence of H.pylori or EBV infection. Therefore, in this study we investigated TP53 and Bcl-2 expression in GC in patients with H.pylori/EBV or without H.pylori/EBV infection.

Methods: The studies were conducted on 52 adult patients with gastric adenocarcinomas: 16 with H.pylori (cagA+)-positivity (group 1), 14 with EBV-positive tumours (group 2) and 22 with H.pylori/EBV-negative tumours (group 3). H.pylori presence in gastric tumour specimens was detected using Giemsa staining and bacterial culture technique. Moreover, cagA gene was detected using PCR. EBV was detected based on EBER presence by RNA in situ hybridization. Expressions of TP53 and Bcl-2 proteins were analysed using immunohistochemistry.

Results: Expression of TP53 was noted in 14 (84%) patients from group 1, 8 (57%) patients from group 2 and 19 (86%) patients from group 3, whereas expression of Bcl-2 was noted in 12 (75%) patients from group 1, in 10 (71%) patients from group 2, and 6 (27%) patients from group 3.

Conclusions: The obtained results permit to conclude that H.pylori (cagA+)-associated development of the gastric adenocarcinoma is determined by abnormalities in the p53 gene function and overexpression of anti-apoptotic Bcl-2, whereas EBV-associated adenocarcinomas seem to be dependent only on the function of bcl-2 pathway.

Abstract no.: P03.12

HELICOBACTER PYLORI VACA AND CAGA GENOTYPES AND THEIR CORRELATION WITH GASTRITIS AND PEPTIC ULCERS IN IRANIAN PATIENTS

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Helicobacter pylori infection is the major cause of gastroduodenal diseases. The development of severe H.pylori disease is evaluated by virulence of infecting strain. Here we determined the association between the vacA and cagA of H.pylori and gastroduodenal diseases in Iranian patients. Gastric biopsy specimens from antrum of 233 dyspeptic patients were cultured. The vacA and cagA genotypes of strains were determined by PCR and sequencing. It was found that the prevalence of vacA s1 was 82%, s1a 74.2%, s1b 7.7%, s2 18%, m1 29.6%, m1a 76.8%, m1b 23.2%, m2 69.5% and cagA gene 71.2%. The vacA s1 genotype was more frequent in isolates from PU patients (108/120, 90%) than in those from gastritis patients (83/113, 73.4%). The s2 allele exhibited higher frequency in isolates from gastritis patients (30/113, 26.5%) than in those from PU patients (12/120, 10%). There wasn't a significant difference between the frequencies of vacA m1 or m2 genotypes and cagA gene in the isolates from PU patients and in those from gastritis patients. VacA s1 m2 was the most frequent in Iranian patients (127/233, 54.5%). The vacA s2 m2 (24/113, 21.2%) and vacA s2 cagA+ (23/113, 20.4%) were more frequent in the isolates from gastritis patients than in those from PU patients (11/120, 9.2%). Furthermore only the vacA s1 genotype showed a strong association with the PUD and vacA s2 m2 and vacA s2 cagA+ were more frequent in the isolates from gastritis patients but vacA s1 m2 cagA+ were more frequent in isolated from PUD.

Abstract no.: P03.13

INTERACTION BETWEEN *H. PYLORI* VACA ALLELES AND AGE OR GENDER OF PATIENTS IN DEVELOPMENT OF CLINICAL OUTCOMES

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Helicobacter pylori major cause of peptic ulcers and gastric cancer is common in Iran. The host, environmental and bacterial factors are involved in H.pylori pathogenesis. The vacA is one of the most important determinants of H.pylori virulence .The aim was to determine the genotypes of H.pylori isolates vacA alleles in relationship between age, gender and their association with clinical outcomes. Biopsies were taken from 233 patients with gastroduodenal diseases referred to the Endoscopy unite of Shariati hospital,, Tehran, Iran. Biopsies were cultured on Brucella Blood agar supplemented with antibiotics. The vacA genotypes of H.pylori strains were determined by PCR and sequencing. Patients were classified into 113 with gastritis, 64 gastric ulcer and 56 duodenal ulcer. Patients were classified into 2 age groups; < 40: 28% and >40: 72%. Gastroduodenal diseases were more prevalent among patients >40. From 76 females >40, 54% had G,33% GU and 13% DU. From 91 males >40, 32% had G,36% GU and 32% DU. The vacA s1 was more in H.pylori isolates from Du (98.2%) than in those from gastritis(73.4%) and vacA s2 exhibited higher frequency in gastritis (26.5%) than in DU(1.7%).The frequency of vacA m2 in male DU patients >40 (46.2%) was higher than females (7.7%).Results revealed that considering the impact of age and gender, in GU patients only age >40 is determinant factor but in DU, male gender. So in Du group there was a significant relationship between vacA s1 and the vacA m2 allele was associated with male patients >40.

Abstract no.: P03.14

H.PYLORI INFECTION IN MONGOLIA AND THEIR VIRULENCE FACTORS

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Background and aim: *H.pylori* infection is associated with different digestive diseases, such as gastritis, peptic ulcer, mucosa-associated lymphoid tissue lymphoma, and gastric cancer. In Mongolia the infection prevalence of H.pylori has been reported in 40–80%. The detection of bacterial isolation have not been identified, therefore aim of study was to determine *H. pylori* strains isolated from Mongolians and detect virulent properties of them.

Materials and method: A total of 320 consecutive patients were enrolled in 2010–2013. All patients underwent upper gastrointestinal endoscopy. Gastric biopsy specimens were tested for the Urease test and for *H. pylori* culture. The culture was performed in microaerophilic conditions at 37°C for a maximum of 5–7 days. Colonies were identified as *H. pylori* according to standard criteria including negative Gram staining, typical cell morphology, and positive reactions to catalase, oxidase, and urease. Genomic DNA was extracted. In serum were detected virulent factors as a Cag A, VacA, GroEl, UreA, HcpC and gGT by RIDA®LINE Helicobacter IgG test.

Results: CLO test yielded positive results for 65.6% [95% CI 60.7–71.0] Among CLO test-positive patients were identified antigen 72% [95% CI 62.1–79.2] positive in fecus, and antigen 68% [95% CI 58.8–77.2] positive in serum. The virulence factors were observed as a Cag A in 95% (57), VacA in 50% (30), GroEl in 80% (48), UreA in 15% (9), HcpC in 68.3% (41) and gGT in 60% (36).

Conclution: The prevalence of H.pylori infection increased among Mongolian population, and the H.pylori phenotype 1 is identified in 48.3% (CagA+VacA).

P04 Epidemiology and Transmission

Abstract no.: P04.01

A QUESTIONNAIRE SURVEY TO DETERMINE THE LEVELS OF KNOWLEDGE AND AWARENESS ABOUT *HELICOBACTER PYLORI* INFECTION FOR STUDENTS AT DOKUZ EYLUL UNIVERSITY HEALTH CAMPUS

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Aim: To assess and compare the knowledge and awareness levels of students in Faculties of Medicine and Nursing, School of Physical Therapy and Rehabilitation(FTR) about *Helicobacter pylori* infection.

Methods: The questionnaire was prepared by the Second Year Medical School Students of Special Study Module at Dokuz Eylül University, Faculty of Medicine,Helicobacter Laboratory of Medical Microbiology Department between October2013-May2014. The questionnaire was consisted of 35 questions including basic knowledge for *H. pylori* infection, medical history for *H. pylori* infection (symptoms,diagnosis, eradication therapy), life standards, personal behaviors for hygiene. Three-hundred-twenty-nine students (171medical, 89nursing, 69FTR students) (146M,183F,mean age,21.3 ± 1.8) were determined by stratified-sampling-method. t-test,ANOVA and χ^2 test were used(SPSS Version 15.0). Scoring were applied to only 12 questions related to the level of knowledge and an index was developed.

Results: Statistical difference was found between Faculties, the highest score was obtained in medstudents (24.5 ± 23.6) according to scored questions. However, the knowledge and awareness levels increased in concordance with parents educations and higher classes.No statistical difference was found between genders ($p = 0.264$). Peptic ulcer and gastric cancer histories in families were determined as 31.6% and 10% of students,respectively. Ten(47.6%) of 21 students who were examined for *H.pylori* infection, were admitted to upper endoscopy and 8(38.1%) had eradication therapy but they did not give any information about which therapy was used. Personal behaviors for hygiene were also determined for 329 students:63.8% don't share their spoon and fork, 77.8% wash their hands before meals, 98.2% wash their hands after toilets, 62.6% clean vegetable and fruits before eating.

Conclusion: Students of health campus had low basic knowledge about *H.pylori* infection therefore there is a need to promote education and awareness of *H.pylori* infection with seminars/lectures.

Abstract no.: P04.02

VARIATIONS IN THE PREVALENCE OF *HELICOBACTER PYLORI* INFECTION IN NORTHERN SARDINIA IN THE LAST 15 YEARS

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Background: The prevalence of H pylori infection varies between and within populations, and is typically acquired in childhood when standards of living were lower (a birth cohort phenomenon).

Aim: To investigate the prevalence variation of H pylori infection in a cohort of patients that underwent upper endoscopy for dyspeptic symptoms.

Methods: This was a retrospective observational study. Patient records scheduled for upper endoscopy were acquired. Only patients with gastric histology available for H pylori identification and 13C-UBT or rapid urease test from 1995 until 2012 were included.

Results: A total of 11360 records were analyzed. In 1467 patients gastric biopsies were not available. The prevalence of H pylori infection was 43% (4300/9893; M: 43% and F: 42%). A significant decline in prevalence was observed from 1995 to 2011 (52% vs 14%; $p = 0.0$). Difference in prevalence was more consistent between age-specific groups of 0–19 years and 60–69 years: 17% versus 44%. A statistical significant difference was observed within each social class for the age specific groups.

Conclusion: The change in the prevalence of H pylori within 15 years among the Sardinian dyspeptic patients is an example of how sensitive H pylori acquisition is to improvement in standards of living. The increased use of anti-H pylori eradication therapy may also play an important role in the reduction of the prevalence.

Abstract no.: P04.03

This abstract has been withdrawn.

Abstract no.: P04.04

MICROBIAL-ECOLOGICAL STUDY ON COLONIZATION OF HUMAN *H. PYLORI* ISOLATES FROM FATHER, MOTHER AND 3 CHILDREN OF A FAMILY IN GASTRIC MUCOSA OF MONGOLIAN GERBIL

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We have already reported multilocus sequence typing (MLST) of DNA from faecal specimens for analysis of intra-familiar transmission of *H. pylori* (Osaki et al., 2013). In the present study, colonization activity of *H. pylori* strains isolated from father (K21), mother (K22) and 3 children (K23–K25) of a family in gastric mucosa of Mongolian gerbil was examined. MLST analysis indicated that sequencing types (STs) of K21, K22 and K23–25 were ST2760, 2761 and 2762, respectively, indicating that 3 strains from siblings had an identical ST.

Mongolian gerbils were inoculated with *H. pylori* K21 or K22 at 1st inoculation and also inoculated with *H. pylori* K25 at 2nd inoculation 10 days after 1st inoculation. An opposite inoculation order experiment was also done. Five weeks after 2nd inoculation, gastric *H. pylori* were cultured from Mongolian gerbil stomach. Bacterial DNA was extracted from each colony and analyzed by RAPD fingerprinting and direct-sequencing of trpC.

All colonies were determined as the same molecular type of K25 in four group gerbils. In these results, the *H. pylori* K25 was more dominant in Mongolian gerbil infection than father- and mother-originated strains, suggesting that colonization activity of the strain is important for intra-familiar transmission of *H. pylori*.

Abstract no.: P04.05

THE IMPACT OF LIFESTYLE FACTORS ON THE RISK OF GASTRIC CANCER IN A CROSS SECTIONAL STUDY

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Background: Variation in cancer incidence in geographical locations is partly owed to diverse lifestyle factors. Among these modifiable dietary habits require more detailed investigations.

Methods: Personal interviews with 559 gastric cancer (GC) and 811 non-ulcer dyspeptic (NUD) patients using comprehensive questionnaires produced extensive information regarding demographic and lifestyle factors prior to disease acquisition.

Results: Multiple logistic regression adjusting for potential confounders revealed the following subjects at increased risk of GC: Ever smokers (OR = 2.10, CI = 1.30–3.35, $p = 0.002$), particularly of the noncardia type GC (OR = 2.11, CI = 1.14–3.93, $p = 0.018$); high salt consumption (OR = 2.10, CI = 1.07–3.94, $p = 0.03$), mainly of cardia type GC (OR = 6.14, CI = 1.40–26.91, $p = 0.016$); smoked food consumption in (OR = 2.98, CI = 1.145–7.75, $p = 0.025$) for cardia type GC; consumption of pickled food (OR = 2.03, CI = 1.13–3.66, $p = 0.018$), particularly in cardia type GC (OR = 3.37, CI = 1.42–8.01, $p = 0.006$), drinking unpurified water (OR = 3.38, CI = 1.17–9.73, $p = 0.024$), particularly in cardia type GC (OR = 14.00, CI = 2.68–73.25, $p = 0.002$); consumption of butter (OR = 4.47, CI = 1.738084–11.49834, $p = 0.002$), particularly in cardia type GC (OR = 8.93, CI = 0.77–105.48, $p = 0.08$); drinking hot tea (OR =3.06, CI = 1.96–4.77, $p = 0.0001$); consumption of processed food (OR = 2.74, CI = 0.99–7.60, $p = 0.053$), particularly in cardia type GC (OR = 7.86, CI = 1.13–54.63, $p = 0.037$); consumption of saturated cooking oil (OR = 3.80, CI = 2.19–

6.57, $p = 0.0001$), particularly in cardia type GC (OR = 5.65, CI = 2.11–15.17, $p = 0.001$). Furthermore, subjects with a family history of GC were at a minimum 3.5 folds increased risk (CI = 1.87–6.43, $p = 0.0001$), particularly of cardia type GC (OR = 6.13, CI = 2.49–15.09, $p = 0.0001$).

Conclusion: Dietary behaviors greatly impact the risk of gastric cancer, particularly of the proximal region. These factors and their healthy alternative recommendations should be taken into serious consideration and publicly propagated.

Abstract no.: P04.06

THE PREVALENCE OF ULCER DISEASES IN EUROPOIDS OF RUSSIA: IS THERE TENDENCY TO DECREASE?

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Aim: Investigate the prevalence of peptic ulcer disease in the population of different regions of Siberia.

Methods: Representative groups were selected by epidemiological method, clinical examination and fibrogastroduodenoscopy for diagnosis of peptic ulcer were performed in 1177 adult Europoids (581 women, 596 men) in town Dudinka (Taimyr), 564 people (293 women, 271 men) in the rural region (Atamanovo, 100 km to north from Krasnoyarsk) and 657 patients (341 women, 316 men) in Krasnoyarsk city. The average age of examined persons was 38.6 years in Taimyr, 42.4 in Atamanovo and 55.3 in Krasnoyarsk. Determination of *H. pylori* was performed by urease and enzyme immunoassay methods in 472 persons in Dudinka, 507 patients in Atamanovo and all 657 people in Krasnoyarsk.

Results: The prevalence of peptic ulcer disease in Dudinka was 8.2% (4.6% in females and 11.7% in males, $p < 0.001$), in Atamanovo was 9.2% (6.5% in females and 12.2% in males, $p = 0.03$) and in Krasnoyarsk was 8.5% (5.8% in women, 11.3% males, $p = 0.007$). The prevalence of *H. pylori* infection in Dudinka was 93.5%, in Atamanovo – 88.6%, in Krasnoyarsk – 91.1%. Ratio of duodenal ulcer / gastric ulcer was equal, respectively, – 4:1, 3.5:1 and 2.7:1. Risk factors for peptic ulcer disease in all regions were *H. pylori*, tobacco smoking and male gender, for gastric ulcer – increasing age.

Conclusion: Presently there is no reason to consider that the prevalence of risk factors and peptic ulcer disease in Russia is reduced.

Abstract no.: P04.07

IDENTIFICATION OF *HELICOBACTER PYLORI* INSIDE FREE-LIVING AMOEBAE IN WATER SUPPLIES

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Helicobacter pylori which infects more than 50% of the global population, has been detected in water, but its transmission pathway remains unknown. Free-living amoebae (FLA) are ubiquitous pathogens commonly found in water. It has been previously shown that FLA can act as hosts for some pathogens, protecting them, and thus acting as Trojan Horses. Inside FLA, amoeba resisting bacteria are more resistant to adverse conditions.

The aim of this work was to investigate the presence of *H. pylori* cells inside amoebae in drinking and waste water samples from Eastern Spain.

Methods: Nineteen drinking and 31 waste water samples were filtered through 3 µm nitrocellulose filters. Membranes were placed in Non-Nutrient-Agar and the culture was maintained until amoebae were observed. Afterwards, extra-amoebic bacteria were killed using sodium hypochlorite. Samples were treated with propidium monoazide to eliminate exogenous DNA and dead cells. DNA from protozoa was extracted and specific *H. pylori* qPCR was performed.

Results: DNA from *H. pylori* cells inside FLA were identified in 11 out of 50 water samples; 7 in waste water and 4 in drinking water. PMA treatment allowed the detection of DNA from *H. pylori* cells only from the inside of live amoebae.

Conclusions: The combination of sodium hypochlorite treatment prior to analysis with PMA-qPCR is a rapid and specific method to detect *H. pylori* cells inside FLA. Thus, our results demonstrate that FLA may be a *H. pylori* reservoir in water, showing that they could protect the bacterium from disinfection treatments and harsh environmental conditions.

Abstract no.: P04.08

MOLECULAR EVIDENCE FOR PRESENCE OF *HELICOBACTER PYLORI* DNA IN WATER SUPPLIES

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Water can be a risk factor for *Helicobacter pylori* (*H. pylori*) infection but the association between presence of *H. pylori* in water supply and clinical infection in individuals drinking from that supply has not been well documented. Using molecular methods we tested the *H. pylori* DNA presence in water samples (total 353) from four sources (water distribution system, rivers, reservoir drinking water and wells) of Cracow region collected between February and November 2012 and 2013. In concentrated by centrifugation water samples, the PCR methods of DNA for the ureA and cagA virulence genes using primer glmM targeting the ureA and primer cagA targeting the cagA genes were utilized. 65 (18%) water samples out of 353 contained *H. pylori* DNA material. In river samples *H. pylori* DNA and virulence genes cagA were present in 5 samples (5.4%) out of 93 but by glmM only in 1 sample. In water distribution system, the detection of *H. pylori* DNA was 37 (30%) and 16 of cagA in 123 samples tested while by glmM primers this detection was 14, 7, 6 and 2 during the period of July 2012, February, March and October 2013, respectively. In reservoir drinking water and wells, H.pylori DNA were detected in 19 (18.6%) and 9 (25%) samples respectively, out of 102 individuals. We conclude that 1) the presence of *H. pylori* DNA in water depends on source of water and year season, 2) the virulence cagA genes are more frequently detected by cagA primers than by glmM primers (Grant #2011/01/B/NZ/01539).

Abstract no.: P04.09

THE RATE OF *H. PYLORI* INFECTION IN PATIENTS WITH ALLERGIC DISEASES IN UKRAINE

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Background: The data about the relationship between H. *Çylori infection and risk of allergic disease are contradicting. The literature includes both negative and positive connections between H. *Çylori infection and asthma, allergic rhinitis, atopic dermatitis and other allergic diseases.

Aims: To study the rate of H. *Çylori infection in patients with verified allergic disease, to determine and to describe possible interaction between them.

Materials and Methods: Of 160 patients age ranged from 5 to 45 years (the average age 27.1**11.2) with different allergic diseases (asthma, pollinosis, allergic rhinitis and atopic dermatitis) were examined. After taking allergy history, spirometry and allergy testing using immunofluorescence method (ImmunoCAP) were done. After verification of allergic diseases, 13C-Urea Breath Test (13 C-UBT) was performed to all the patients including control subjects (70 healthy people, average age 30.3**12.3) to define their the H. *Çylori-status.

Results: The average infection rate of patients having verified allergic diseases was equaled to 47.7%, and 61.4% – for the control subjects (*á < 0.05). The infection rate in group of patients under 20 years having allergies was 34.2% (control group – 52.8 $p < 0.01$), and after 20 years – 61.2% (control group ΓÇô 70%, *á > 0.05).

Conclusions: The rate of H. *Çylori infection among patients with different allergic diseases, particularly among young patients, is much lower compared to control group. To prove the negative connection between positive H. *Çylori-status and allergies in young patients the further research with larger number of patients is required.

Abstract no.: P04.10

HELICOBACTER PYLORI PREVALENCE IN HIV-INFECTED SUBJECTS WITH DIFFERENT ETHNIC BACKGROUND

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Introduction: The role of *Helicobacter pylori* infection in HIV related upper gastroduodenal morbidity is unclear. Up to now, several studies have reported discrepant results about the prevalence of *H. pylori* in HIV positive subjects.

Aim: The aim of the study was to analyze the prevalence of *H. pylori* infection in HIV-infected subjects. As a control group, we used an age matched group from a previous study conducted in our department.
Material and Methods: We prospectively analyzed the *H. pylori* infection status in 191 HIV positive subjects (45 female) via serology from different countries (Germany: n = 135; Africa: n = 39; Russia: n = 13; Vietnam: n = 3). The control group of HIV-negative subjects consisted of 185 patients.
Results: The mean age of the participants was 40.5 years (±10.83 years SD). The overall prevalence of *H. pylori* was 37.2% (71/191). In female subjects, we detected a higher prevalence (40%) compared to male patients (34%). Interestingly, in patients from Germany the prevalence of *H. pylori* was lower with 28.1% compared to patients from Russia (69.2%) or Africa (61.5%).The overall prevalence of *H. pylori* in HIV positive subjects was comparable to non- infected patients (40.6%) in our region.
Conclusion: There was no difference of *H. pylori* prevalence between HIV positive and negative patients. In HIV patients from countries with a known high prevelance of *H. pylori* we also detected a higher prevalence for *H. pylori*. Those findings are in contrast with previous reports that suggested a lower prevalence of *H. pylori* in patients with HIV.

Abstract no.: P04.11

SURVIVAL STRATEGY OF *HELICOBACTER PYLORI* IN ENVIRONMENTS BY CO-EXISTENCE IN *ACANTHAMOEBA CASTELLANII*

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Helicobacter pylori is a causative agent for gastritis, peptic ulcer diseases and gastric cancer. Almost 50% of the world's populations harbor this bacterium. Transmission route of *H. pylori* is not known, but it is implied that they are distributed in environments because their DNA are detected in river water.
On the other hand, protozoa including free-living amoeba are universally distributed in water and soil. They generally eat various kinds of bacteria, however, some species of bacteria have resistance against digestion system of protozoa. Thus, protozoa are regarded as reservoir of bacteria in environments.
In this study, it was analyzed whether *H. pylori* have resistance against digestion system of protozoa and survive in co-culture with *Acanthamoeba castellanii*.
A. castellanii were cultured with PYG medium until they confluently develop to bottom of 6-well microplate. Approximately 10^9 CFU/ml of *H. pylori* were added to the microplate, and the cultures were centrifuged. The microplates were incubated and the cultures were sampled for CFU assay and morphological examination by scanning electron microscopy (SEM).
Three hours after incubation, the numbers of *H. pylori* were 4.17×10^8 CFU/mL in co-culture with *A. castellanii*, 2.75×10^8 CFU/mL in bacterial single culture. Twenty-four hours after incubation, they were 1.21×10^8 CFU/mL and 2.30×10^5 CFU/mL in co-culture and single culture, respectively. In addition, SEM showed coccoid formation of *H. pylori* in bacterial single culture. The results obtained suggest a possibility that *H. pylori* might survive in co-culture with protozoa.

Abstract no.: P04.12

FOURTEEN YEARS ANNUAL CHANGE OF ERADICATION RATE AND UNEXAMINED (PATIENTS WHO DON'T UNDERGO DIAGNOSIS OF ERADICATION RESULT) RATE IN JAPAN

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Background/Aims: A systematic eradication strategy, proton pump inhibitor/amoxicillin and clarithromycin (PPI/AC) for first line and proton pump inhibitor/amoxicillin and metronidazole (PPI/AM) for second line for H.pylori has been constructed in Japan. However, the spread of eradication therapy, with patient who are not examined the result of therapy might increase. To address this clinical issue in Japan, 14 years annual change of eradication rate and unexamined (patients who don't undergo diagnosis of eradication result) rate was surveyed.
Methods: Patients who received first-line PPI/AC therapy and second-line PPI/AM therapy between 2000 and 2013 were retrospectively analyzed. The annual eradication rate and unexamined rate was calculated. Data were subjected to intention-to-treat analysis.
Results: PPI/AC was administered to 3167 patients and 770 patients received PPI/AM. Eradication rate for PPI/AC regimen was 78.5%, 73.5%, 63.4%, 69.4%,74.4%, 63.4%, 61.5%, 60.1%, 65.4%, 64.8%, 61.7%, 71.3%, 69.6%, 64.2% and unexamined rate was 8.9%, 4.8%, 0.8%, 1.0%, 1.3%, 2.1%, 3.6%, 6.2%, 8.2%, 9.9%, 8.0%, 8.0%, 8.3%, 7.5% in 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013, respectively. Eradication rate for PPI/AM regimen was 80.0%, 77.1%, 71.4%, 78.4%, 91.9%, 82.7%, 86.4%, 89.5%, 84.8%, 85.7%, 83.6%, 82.7%, 80.7%, 76.7% and unexamined rate was 6.7%, 0%, 0%, 5.4%, 2.7%, 3.8%, 6.8%, 1.8%, 2.6%, 3.9%, 4.9%, 12.0%, 5.3%, 14.6%, respectively.
Conclusion: Since unexamined rate becomes serious issue in clinical practice in Japan, physicians should aware this issue and deal with to reduce unexamined patients.

Abstract no.: P04.13

PREVALENCE OF GASTROINTESTINAL SYMPTOMS AND *H. PYLORI* INFECTION IN A LARGE PHILIPINO COMMUNITY IN ROME: RELATIONSHIP WITH LIFESTYLE HABITS

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Background and Aim: Philipino population is largely represented in Italy, generally arranged in large communities of friends and/or relatives, usually maintaining the traditional Philipino lifestyle. However, some of them acquired Western habits. Our aim is to investigate prevalence of gastrointestinal symptoms and *H. pylori* infection in a Philipino community in Rome
Methods: Our population was a 600-subjects Philipino community established in Rome since 2004. *H. pylori* was assessed by C13 Urea Breath Test. Gastrointestinal symptoms were investigated through a symptom questionnaire.
Results: 580 subjects were available for interview, grouped according to age: 52 < 16 yo; 210 between 16 and 35 yo; 270 between 35 and 55 yo and 43 > 55 yo. 80% keep the traditional Philipino dietary habits, were free from alcohol and smoke, whereas 20% acquired a Western dietary lifestyle together with alcohol and smoke consumption. 25 subjects complained of abdominal pain; all of them had a Western lifestyle. Bowels were regular in all except 20 subjects. 60 complained of headache. Bloating was found in 70 subjects, whereas 30 (consuming coffee and cold sparkling beverages) complained of reflux symptoms. All subjects have a spicy diet. *H. pylori* was found in 19 out of 25 subjects complaining of abdominal pain and in only 1 out of 25 random subjects (comparable for age and gender) without abdominal pain ($p < 0.0001$).
Conclusions: In our study, investigating a large Philipino community living in Italy, lifestyle and dietary habits appear to have a more relevant role than genetics in the development of gastrointestinal symptoms and *H. pylori* infection.

Abstract no.: P04.14

THE INFLUENCE OF GENDER AND AGE OF DYSPEPTIC PATIENTS ON THE DEVELOPMENT OF PEPTIC DISEASES

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Aim: To determine the role of gender and age in the development of peptic diseases in *Helicobacter pylori* (HP)-positive patients.
Methods: Gastric biopsies were taken from 628 dyspeptic patients. Rapid urease test was performed. Patients were classified according to peptic diseases, gender and age.
Result: Positive rapid urease activity indicated that 213 /628 (33.91%)patients had HP infection. Among these patients 188(88.26%) had gastritis; 83(44.15%) males (52 ≥ 40 and 31 < 40) and 105(55.85%) females (67 ≥ 40 and 38 < 40), 23(10.79%) had peptic ulcers; 16 males (15 ≥ 40 and 1 < 40) and seven females (3 ≥ 40 and 4 < 40) and 2(0.93%) males ≥40 had gastritic cancer.
Discussion: There was a considerable reduction in HP-positive patients (% 33.91) compared with previous studies in Iran (69%- 89%). Among HP-positive patients 88.26% had gastritis with females ≥40 comprising 35.63% of patients. Patients with peptic ulcer comprised 10.80% with males ≥40 comprising 65.21% of patients. The two cancer patients were also men and ≥ 40 years old. It appears that old age is the primary determinant risk factor involved in peptic diseases. Furthermore, male gender increases the risk for PU and cancer.

Abstract no.: P04.15

PREVALENCE OF *HELICOBACTER PYLORI* INFECTION IN VINNYTSIA (UKRAINE)

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Background: In Ukraine there is a reduction of morbidity diseases closely related to *Helicobacter pylori* (HP). For example, in Vinnytsia oblast crude incidence rate of stomach cancer per 100 000 of population decreased from 30.0 in 2004 to 27.2 in 2012.
Methods: The study was conducted from 2007 to 2013 on people (7–84 years old) never received HP eradication. Most of them had dyspeptic complaints (78.4%) or halitosis (3.8%). 13C-urea breath tests were performed with infrared spectrometer (IRIS, Wagner Analysen Technik). The protocol provided intaking 75 mg of urea in the sour juice. The cutoff point for classifying cases as positive was >3.5% DOB (delta over base).
Result: In 2007–2008 among 106 men and 116 women (mean age (±S.E.M.) of 39.17 ± 1.05 y.o.) 62.61% were HP-positive. In 2009–2010 among 55 men and 64 women (mean age of 36.75 ± 1.34 y.o.) 49.58% were HP-positive. In 2011–2012 among 76 men and 105 women (mean age of 39.57 ± 1.12 y.o.) 42.54% were HP-positive. In 2013 among 40 men and 49 women (mean age of 41.48 ± 1.84 y.o.) 42.2% were HP-positive.
Conclusion: In recent years HP-infection rate decreased significantly in Vinnytsia region. The most likely reasons for this decline are the active promotion of eradication therapy by general practitioners and improving the welfare of the population.

Abstract no.: P04.16

HELICOBACTER PYLORI BIOFILM – THE PROBABLE MODE AND SOURCE OF TRANSMISSION?

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The detection of *Helicobacter pylori* by molecular approaches in water sources has led to the postulation that the bacterium may survive in the extragastric environment. But the exact route and mode of its transmission still remains elusive. Preliminary finding of *H. pylori*-specific 16S rDNA in ready-to-eat food collected from different food sources indicates that food samples may be a vital link to the probable existence of *H. pylori* in various other environmental sources. In addition, observations from scanning electron and confocal laser micrographs showed that the bacteria were able to reside on the lettuce surfaces, forming biofilm, strengthening the possible survival of *H. pylori* in food. It also suggests that biofilm may play an important role in the survival strategy of *H. pylori* in this extragastric environment. Furthermore, our in vitro study shows that the biofilm forming ability of various Asian *H. pylori* isolates is strain dependent. This implies the variability in ability of *H. pylori* in colonizing on different food sources. As such, *H. pylori*-contaminated food can be a cause for public health concern. Interestingly, SEM analysis of gastric biopsies also revealed the attachment of such biofilm-like structure on the gastric mucosa of *H. pylori*-infected patients, an indication that *H. pylori* is capable of adapting to the biofilm state so as to thrive in or overcome the unfavourable gastric environment. Taken together, food may serve as a possible source for the transmission of *H. pylori* and that biofilm may play a role in the process of *H. pylori*-associated infections.

Abstract no.: P04.17

This abstract has been withdrawn.

Abstract no.: P04.18

THE PROPORTION OF *HELICOBACTER PYLORI* TESTING IN PATIENTS WITH PEPTIC ULCER BLEEDING: SINGLE CENTER EXPERIENCE

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Background: The use of NSAIDs and *Helicobacter pylori* infection are major cause of peptic ulcer disease. Peptic ulcer bleeding still remains a common medical Illness associated with morbidity and mortality. The aim of this study was to clarify the proportion of patients with peptic ulcer bleeding who had *Helicobacter pylori* testing and prevalence of *Helicobacter pylori* infection in patient with peptic ulcer bleeding.
Methods: Between January 2010 and April 2014, 89 patients received emergency esophagogastroduodenoscopy due to peptic ulcer bleeding. NSAIDs induced ulcer bleeding was defined as peptic ulcer bleeding diagnosed on the basis of endoscopic findings in patients who take a NSAIDs medication. *Helicobacter pylori* infection was detected using rapid urease test and histology.
Results: Among 89 patients, 74 patients were males (83.1%) and mean age was 60.21 ± 18.1 years. 30 patients (33.7%) took NSAIDs. Rapid urease test was performed in 68 patients (76.4%). Endoscopic biopsy was performed in 49 patients (55.1%). Patients with non-NSAIDs group had significantly lesser rapid urease test than NSAIDs group (41 (69.5%) vs 27 (90%), $p = 0.031$). The prevalence of *Helicobacter pylori* infection in patients with Peptic ulcer bleeding was 40%.
Conclusions: Among patients with peptic ulcer bleeding, *Helicobacter pylori* testing was perfomed in 78% of patients. However, The proportion of patients who had *Helicobacter pylori* testing in non-NSAID group was significantly lesser than NSAIDs group (69.5% vs 90%, $p = 0.031$). In patients with non-NSAIDs group, Efforts to increase *Helicobacter pylori* testing are needed to reveal etiologies.

Abstract no.: P04.19

SEROPREVALENCE OF *HELICOBACTER PYLORI* IN CHILDREN IN A RURAL AREA

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BACKGROUND *Helicobacter pylori* (Hp) infection has been recognized as a cause of chronic gastritis, peptic ulcer, atrophic gastritis and gastric cancer.
Aim: To analyzed the seroprevalence of *Helicobacter pylori* in pediatric age in rural area and to evaluate some epidemiologic characteristics.
Patients and Methods: The study included 100 patients (80 males; age range 5–13 years) suffering from different gastrointestinal complaints. Blood serology and stool antigen testing
were used for the diagnosis of infection due to *H. pylori*. We interviewed the children with questionnaire about socioeconomics factors, hygiene, living conditions and their dietary habits.
RESULTS 20 (20%) of the 100 patients were positive for *Helicobacter pylori* and this positivity had a significantly increasing correlation with age ($p < 0.001$). A lower frequency of fermented dairy food, fruits and vegetable consumption was registred among infected children. Among infected patients were noted low socio-economic markers such as croweded living conditions and unclean water.
Conclusions: Might decrease the risk of Hp infection the use of vitamin C and antioxidants contained in fruit and vegetables.
Risk factors for Hp infection are low socioeconomics factors, hygiene and living conditions.

P05 Inflammation and Host Response

Abstract no.: P05.01

ROLE OF HPYAVIBM GENE (HP0051) OF *HELICOBACTER PYLORI* IN VIRULENCE

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Helicobacter pylori, a human pathogen, colonizes in stomach and causes gasroduodenal problems. By modulating different interactional mechanisms, *H. pylori* evades host immune response. The bacterial genome consists of numerous restriction-modification genes but the relevance of having such huge number of genes is still unclear. It is now established that N6-adenine methylation plays a crucial role in bacterial gene regulation and virulence but not much is known about the effect of C5-cytosine methylation on these aspects. In this study we have examined the influence of an orphan cytosine methyltransferase, hpyAVIBM on gastric infection in mice and cultured cells. Histopathological staining showed that deletion of this hpyAVIBM gene in *H. pylori* strain (SS1) has more damaging haemorrhagic effects on mice stomach. The gelatin-zymography result demonstrated that the mice infected with mutant *H. pylori* strain (SS1ΔhpyAVIBM) had significant up-regulation of pro-MMP-9 than those infected with wild type bacteria. In addition, ELISA results of pro-inflammatory cytokines (IL-6 and IL-1β) also proved that mutant strain had more inflammatory effect on mice stomach than its counterpart. Immunohistochemistry data also suggested that mutant strain was causing more epithelial cell damage. Cell culture studies revealed that this SS1ΔhpyAVIBM strain caused more apoptosis in AGS cells compared to the SS1 strain. Knockout strain induced strong immune response as monitored by higher pro-inflammatory cytokines induction, probably because of the up-regulation of various virulence factors. Our data indicated that DNA methylation by this methylase could be playing a critical role in modulating virulence and its interaction with the host.

Abstract no.: P05.02

ERADICATION THERAPY HAS NO IMPACT ON INSULIN RESISTANCE ASSESSED WITH HOMA-IR IN KOREAN PATIENTS WITH *HELICOBACTER PYLORI* INFECTION

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Background/Aim: Several epidemiological studies proposed an association between *Helicobacter pylori* (*H. pylori*) infection with insulin resistance. However, there is no conclusive evidence regarding this association. The aim of this study was to clarify the influence of *H. pylori* eradication treatment on insulin resistance in Korean patients. Methods: In this prospective single-armed longitudinal study, 126 patients underwent endoscopy and *H. pylori* testing. All of the 84 *H. pylori*-positive patients received eradication therapy. Among 52 patients who were followed up, therapeutic success was observed in 39 patients (75%). Metabolic parameters including HOMA-IR level were measured at baseline in all patients and 16 weeks after eradication therapy in those initially positive for *H. pylori*. Results: Baseline demographic and anthropometric characteristics were not significantly different between the *H. pylori*-positive (n = 84) and *H. pylori*-negative subjects (n = 42). Serum HDL (50.9 ± 2.1 vs 58.3 ± 3.0 mg/dL, $p = 0.044$) and TG levels (177.8 ± 7.9 vs 153.6 ± 6.3 mg/dL, $p = 0.033$) were different between *H. pylori*-positive and negative subjects. Between two groups, there was no difference in HOMA-IR level (1.98 ± 0.09 vs 1.94 ± 0.09, $p = 0.821$). After eradication therapy, changes in the serum levels of metabolic parameters were similar between eradication success (n = 39) and failure groups (n = 13). No significant changes from the baseline in metabolic parameters within group with successful eradication, including HOMA-IR level (1.97 ± 0.12 vs 1.95 ± 0.11, $p = 0.449$), were observed. Proportion of patients with insulin resistance was not significantly changed from baseline (30.8% vs 29.6%, $p = 0.802$) Conclusion: Metabolic parameters associated with insulin resistance, including HOMA-IR level, were not changed after *H. pylori* eradication treatment in Korean patients.

Abstract no.: P05.03

CHEMOKINES AND ANTIMICROBIAL PEPTIDES CAG-DEPENDENT EARLY RESPONSE TO *HELICOBACTER PYLORI* INFECTION IN PRIMARY HUMAN GASTRIC EPITHELIAL CELLS

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Helicobacter pylori infection systematically causes chronic gastric inflammation that can persist asymptomatically or evolve towards more severe gastroduodenal pathologies such as ulcer, MALT lymphoma or gastric cancer. The cag pathogenicity island (cag-PAI) of *H. pylori* allows for translocation of the virulent protein CagA and fragments of peptidoglycan into host cells, thereby inducing the production of chemokines, cytokines and antimicrobial peptides. In order to characterize the inflammatory response to *H. pylori*, a new experimental protocol for isolating and culturing primary human gastric epithelial cells was established using pieces of stomach from patients who underwent sleeve gastrectomy. Isolated cells expressed markers indicating that they were mucin-secreting epithelial cells. Challenge of primary epithelial cells with *H. pylori* B128 underscored early dose-dependent induction of mRNA expression of the inflammatory mediators CXCL1-3, CXCL5, CXCL8, CCL20, BD2 and TNFα. In AGS cells, significant expression of only CXCL5 and CXCL8 was observed following infection suggesting that these cells were less reactive than primary epithelial cells. Infection of both cellular models with H.pylori B128ΔcagM, a cag-PAI mutant, resulted in weak inflammatory mediator mRNA induction. At 24 hours post-infection of primary epithelial cells with *H. pylori*, inflammatory mediator production was largely due to cag-PAI-substrate-independent virulence factors. Thus, *H. pylori* cag-PAI substrate appears to be involved in eliciting an epithelial response during the early phases of infection. Afterwards, other virulence factors of the bacterium take over in development of the inflammatory response. Using a relevant cellular model, this study provides new information on the modulation of inflammation during *H. pylori* infection.

Abstract no.: P05.04

TLR2 GENETIC POLYMORPHISM ON THE RISK OF *HELICOBACTER PYLORI* INFECTION IN DYSPEPTIC BRAZILIAN PATIENTS

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Inflammation is a primary defense against various extracellular stimuli, such as *Helicobacter pylori* infection in the gastric mucosa.Polymorphisms in genes Toll-like, as TLR2 seem to play a role in susceptibility to inflammatory diseases and cancer. The aim of this study was to evaluate the association of the TLR2 19216 T/C on the risk of *H. pylori*-Hp infection using the PCR-RFLP technique in 140 Brazilian individuals (70 Hp positive patients – 37 males and 33 females; and 70 Hp negative- 28 males and 42 females). The Fisher's Exact Test was conducted to examine whether the genotype frequencies were in Hardy-Weinberg equilibrium. Multiple logistic regression analysis was conducted using the co-dominant, dominant and recessive models, p-values< 0.05 were considered statistically significant. For the Hp positive group, the genotype frequencies for TT, TC and CC were 39.1, 49.3 and 11.6%, respectively, while the allelic frequencies for T and C were 63.7% and 36.3%. For the Hp negative group, the genotype frequencies for TT, TC and CC were 26.9, 49.2 and 23.9%, respectively, while the allelic frequencies for T and C were 51.5 and 48.5%. The multiple logistic regression showed that the polymorphic variant TLR2 19216 CC in the co-dominant model (OR = 0.48, 95% IC = 0.23–0.98, $p = 0.04$) was associated with a protection on the risk of H.pylori infection in dyspeptic. Our data indicate that polymorphism in TLR2 19216 T/C may decrease the risk of *H. pylori* infection in the Brazilian population, reinforcing the important role of inflammatory process in gastric carcinogenesis.

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Abstract no.: P05.05

ETHYL PYRUVATE REDUCED *H. PYLORI*-INDUCED INFLAMMATION THROUGH INHIBITION OF HMGB1/TLR4 PATHWAYS

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Background: High mobility group box 1 (HMGB1), an endogenous ligand of toll-like receptor 4 (TLR4), contributes to pathogenesis of many diverse inflammatory disorders, but their roles in *H.pylori* infection are still unclear. This study intends to explore the effect of ethyl pyruvate (EP), a HMGB1 inhibitor, on expressions of HMGB1/TLR4 pathways in GES-1 and THP-1 cells induced by *H.pylori* infection, and release of pro-inflammatory cytokines.
Methods: ①GES-1 were co-culturing with *H. pylori* for different time (0, 3, 6, 12, 24 and 48 hours) at different bacteria/cell ratio (MOI) (MOI = 0, 10, 25, 50, 100 and 200); ②Pretreated for 1 hour with EP at 5 mmol/L, GES-1 were co-cultured with *H.pylori* at MOI = 100.Then GES-1 and THP-1 cells were co-culturing with trans-well system for 24 hours. The cells and culture supernatant were harvested and subjected to detection for mRNA and protein expressions of HMGB1/TLR4/p-NFκB p65 and release of HMGB1, IL-1βand TNF-α by RT-PCR, western blot and ELISA, respectively.
Results: ①Only at 12 hours, 24 hours and 48 hours, or at MOI = 50, 100 and 200, *H. pylori* infection up-regulated the mRNA and protein expressions of HMGB1/TLR4/p-NFκB p65 in GES-1 cells and increased HMGB1 release; ②EP down-regulated the mRNA and protein expressions of HMGB1/TLR4/p-NFκB p65 in GES-1 and co-cultured THP-1 cells, and decreased the release of HMGB1, IL-1βand TNF-α.
Conclusion: EP reduces *H.pylori*-induced inflammation through inhibition of HMGB1/TLR4/p-NFκB p65 expressions and reduction of HMGB1, IL-1β and TNF-α release.

Abstract no.: P05.06

HUMAN ANTIBODY RESPONSE AGAINST *HELICOBACTER PYLORI* CAGA MAY PLAY A ROLE IN ATHEROSCLEROTIC-RELATED DISEASES THROUGH MOLECULAR MIMICRY MECHANISMS

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Clinical and experimental evidence indicates a significant association between CagA seropositivity and vascular diseases. This correlation could be linked to molecular mimicry mechanisms by which anti-CagA antibodies may recognize human endothelial antigens, therefore interfering with their function. In our work, three N-terminal His6-tagged recombinant fragments of CagA protein were obtained in the native form through application of SUMO fusion expression system. Protein CagA-fr.1 (65 kDa) represents the most conserved N-terminal part of the cytotoxin. Fragment CagA-fr.2 (44 kDa) corresponds to the central conserved region of CagA whereas CagA-fr.3 (39 kDa) represents the highly variable C-terminal region. By means of Ni ++chromatographic purification, high levels of purity (90%) and yield (10 mg/L of culture) of recombinant CagA fragments were achieved. To evaluate patients' immune response against CagA, ELISA were performed using CagAfr.2 as target antigen since it is found to be the most immunogenic fragment. Five sera from patients with unstable plaques showed an antibody titer against CagA higher than Hp positive sera from as many patients with stable vascular disease. A Selected serum with the highest anti CagA titer has then been used for immunoblot assays against self-antigens deriving from coronary plaques total proteins extract showing a reactivity against a 50 kDa antigen yet to be identified. Our preliminary results show that the study of human antibody response against *Helicobacter pylori* CagA can greatly contribute to the understanding of the role played by this important virulence factor in the bacterium-host interplay that may lead to autoimmune responses.

Abstract no.: P05.07

THE INFLUENCE OF TIM-3 ON TLR4 PATHWAYS IN RAW264.7 INFECTED WITH *H. PYLORI*

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Background: Macrophages play an important role in *H.pylori* infection. Toll-like receptor 4 (TLR4) activated macrophages to secrete plenty of cytokines which regulated inflammation and immunity reaction; T-cell immunoglobulin and mucin-domain-containing molecule-3 (Tim-3), an important member of TIM family, was also expressed on macrophages and could impact macrophages function through interacting with TLR4 pathways. Until now, It is unclear that how *H.pylori* impacts Tim-3 and TLR4 pathways in macrophages.
Methods: ①RAW264.7 cells were co-cultured with *H.pylori* SS1 at different bacteria/cell ratio (MOI) at 3, 6, 12, 24 and 48 hours were detected by MTT assay, respectively. At 12 hours, the mRNA expressions of Tim-3\TLR4\MyD88 were measured by RT-PCR; ②Tim-3-overexpressing RAW264.7 cells were constructed by transfer pLVX-IRES-ZsGreen-Tim-3 and co-cultured with *H.pylori*. The mRNA and protein expressions of Tim-3\TLR4\MyD88 were determined by RT-PCR and Western Blot. The concentrations of cytokines (TNF-α, IL-6, IFN-γ and IL-10) in supernatants were measured by ELISA.
Results: ①*H.pylori* stimulation could enhance the proliferation of RAW264.7 at 6, 12 and 48 hours, and elevate the mRNA expressions of Tim-3\TLR4 \MyD88 in RAW264.7 at 12 hours.②*H.pylori* stimulation could up-regulate the expression of Tim-3 in RAW264.7 or in Tim-3-overexpressing RAW264.7. However, the expressions of TLR4\MyD88\p-NF-κBp65 or the release of pro-inflammatory cytokines (TNF-α\IL-6\IFN-γ) were increased in RAW264.7, but not in Tim-3-overexpressing RAW264.7. In the contrast, the level of IL-10 in RAW264.7 or Tim-3-overexpressing RAW264.7 was decreased.
Conclusion: Over-expression of Tim-3 reduces *H.pylori*-induced inflammation through down-regulating TLR4 pathways expressions and pro-inflammatory cytokines release from RAW264.7 infected with *H.pylori*.

Abstract no.: P05.08

CORRELATION OF NOD2 GENOTYPES WITH *HELICOBACTER PYLORI* INFECTION IN A SOUTH-EUROPEAN COUNTRY

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Background: Outcome of *Helicobacter pylori* (Hp) infection results from interaction of multiple variables including host genetic factors.
Aim: This study aimed to investigate if NOD2 genotype increased the risk of *H. pylori* infection and if it has any relationship with bacterial resistance to antibiotics.
Patients and Methods: This prospective study involved 69 patients (HpP) with positive 13C-Urea Breath Test (UBT) and a control group of 249 individuals divided in two groups: dyspeptics with recent, negative, UBT (HpN) – 47; healthy individuals with no study for Hp (HpC) – 202. None of them had history of inflammatory bowel disease. The three main NOD2 mutations (3020insC, R702W and G908R) were obtained by polymerase chain reaction for all involved patients. Hp resistance patterns to antibiotics were determined for 49 infected individuals: clarithromycin – 46.9%; metronidazole – 28.6%; levofloxacin – 34.7%.
Results: Overall, NOD2 mutations were found in 41 individuals (12.9%): HpP – 14.5%; HpN – 8.5%; HpC – 13.4% ($p = 0.606$). Polymorphism R702W was the most frequent (8.2%) followed by G908R (4.4%) and 3020insC (0.9%) with no differences between groups. Comparative subanalysis of groups HpP and HpN also revealed no differences for the presence of mutations (OR = 0.55; 95%CI 0.16–1.87). Such polymorphisms also did not determined increased resistance to clarithromycin (8.7% vs 19.2%; $p = 0.424$), metronidazole (14.3% vs 14.3%; $p = 1$) and levofloxacin (11.8% vs 15.6%; $p = 1$).
Conclusions: NOD2 mutations are not associated with increased risk of Hp infection or resistance of this bacterium to clarithromycin, metronidazole and levofloxacin.

Abstract no.: P05.09

MICROBIAL TRANSLOCATION IS ASSOCIATED WITH ADAPTIVE IMMUNE SENESCENCE AND EXHAUSTION IN HIV+ PATIENTS AFFECTED BY HHV-8-RELATED DISEASES

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Background: Translocation of microbial products (MT) is one of the mechanisms of inflammation during chronic HIV-1 infection. However, its contribu-

tion to T lymphocyte impairment in HIV+ patients (pts) with HHV-8-related diseases has not been determined. Methods
Peripheral blood samples were collected from HIV+ pts at diagnosis of MCD (3 pts), KICS (3 pts), PEL (2 pts) and in IBD (4 pts) as control. 16S rDNA, HIV-1 and HHV-8 DNA levels were measured by quantitative Real Time PCR. Soluble (s)CD14 MT-related marker was measured by ELISA. Parameters of T cell activation (CD38, HLA-DR), senescence (CD28, CD57), exhaustion (PD-1, Tim-3) and CD4 subsets (CXCR3, CCR6, CCR4) were analyzed by flow cytometry. Spearman Rank Test was used for correlations between immunovirologic parameters.
Results: HHV-8 and HIV-1 DNA levels were associated with Th1 ($r = 1$, $p < 0.0001$) and CD8+ PD-1+ lymphocytes ($r = 0.97$, $p = 0.005$). Median levels of sCD14 and 16S rDNA were 2905 ng/mL and 6960 cp/mL in MCD, 1891 ng/mL and 4247 cp/mL in KICS, 2532 ng/mL and 13446 cp/mL in PEL, 1198 ng/mL and 24499 cp/mL in IBD pts, respectively. sCD14 was associated with CD4/CD8 ratio ($r = -0.94$, $p = 0.005$). 16S rDNA was inversely associated with CD4+ Tim-3 + ($r = -0.9$; $p < 0.04$) and directly with senescent CD8 + CD28 + CD57 + cells ($r = 0.9$; $p < 0.04$).
Conclusion: The significative associations of MT markers with CD4 + Tim-3 + and CD8 + CD28 + CD57 + cells supports the hypothesis that increased MT limits the expansion of exhausted lymphocytes and promotes premature immunosenescence. High MT levels might contribute to the pathogenesis of HHV-8 related diseases by imbalancing T lymphocytes responses.

Abstract no.: P05.10

CLINICAL RELEVANCE OF TYPE A GASTRITIS WITH *HELICOBACTER PYLORI* INFECTION

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Introduction: *Helicobacter pylori* (*H. pylori*) infection is related with gastric diseases such as gastritis, peptic ulcers, MALT lymphoma and gastric cancer. *H. pylori*-infected patients develop atrophy of the body mucosa and gastric ulcer. *H. pylori* infection also cause hypergastrinemia and duodenal ulcer. Type A gastritis also cause body dominant gastritis and atrophic change. The aim of this study investigate the role of type A gastritis in pathogenesis of *H. pylori* related gastric ulcer and duodenal ulcer.
Patients and methods: In 212 outpatients referred to Youido St. Mary's Hospital, endoscopy was performed. *Hp* status was identified by biopsy specimens that were stained Warthin-Starry stain and/or urea breath test. Fasting serum pepsinogen I, II, gastrin and anti-parietal cell antibody(APCA) were checked
Results: The fasting serum gastrin level of APCA positive patients was significantly higer than APCA negative patients (121.2 ± 27.1 pg/mL vs 65.8 ± 4.3 pg/mL, $p < 0.05$). The fasting serum gastrin level of *Hp* positive patients was not different with *Hp* negative patients(83.9 ± 10.9 pg/mL vs 68.2 ± 6.2 pg/mL, p = NS). In gastritis patients, prevalence rate of type A gastritis and type B gastritis were 20.8%(22/106) and 40.6%(43/106). The prevalence rate of APCA positive patients were significantly higher in gastric ulcer than in duodenal ulcer(28.0% vs. 11.1%, $p < 0.05$). But prevalence rate of *Hp* positive patients were not different in gastric ulcer and duodenal ulcer(60.0% vs. 77.8%, p = NS).
Conclusion: With this results, type A gastritis patients had a significant higher level of gastrin and develop gastric ulcer rather than duodenal ulcer.

Abstract no.: P05.11

THE LEVEL OF TUMOR NECROSIS FACTOR α FROM PATIENTS WITH INFECTED OF *HELICOBACTER PYLORI*

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Aim: To determine the level of TNFα in serum with *H. pylori*-infections.
The objects of the research were gastric biopsy materials from 100 patients (Khakas – 48, Caucasians -52) with duodenal ulcer (DU), 128 patients (Khakas – 68, Caucasians – 60) with chronic gastritis (CG). All the patients had *H. pylori* positive carrier state. A control group was made of almost healthy donors *H. pylori* negative takes (Khakas – 30, Caucasians – 30). The level of TNFα were determined in serum by ELISA (Vector-Best, Novosibirsk).
In patients with CG and DU TNFα concentration in serum was significantly higher than in controls. In Caucasians patients with CG content TNFα was 1180.0 (870.0–1900.0) pg/ml in patients with DU – 980.0 (416.0–1570.0) pg/ml. In healthy donor concentrations were at the level of interleukin 54.0 (26.0–59.0) pg/ml, $p < 0.05$. At the Khakases TNFα content was: 1210.0 (490.0–2130.0) pg/ml with CG and 1310.0 (580.0–2200.0) pg/ml in patients with DU. The level of TNFα in the serum of healthy donors (41.5 (33.0–50.0) pg/ml, $p < 0.05$). The level of cytokine content was found as follows: at DU TNFα concentration in serum was significantly higher in Khakases than in Caucasians.
Thus, the differences can be established between interleukin content at the Khakases and the Caucasians as the basis for the formation of a personalized approach to the diagnosis of *H. pylori* associated diseases based on ethno-population characteristics.

Abstract no.: P05.12

THE LEVEL OF CYTOKINES IN SERUM INFECTED WITH *HELICOBACTER PYLORI*

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The main aim: To determine the level of IL-17, IL-2 and INF-γ in serum with *H. pylori*-infections.
Material and methods: Of 31 people Caucasian population in the age from 19 to 26 years of age were studied. All respondents were relatively healthy. The titer of antibodies specific to *H. pylori* and level of IL-17, IL-2, IFN-γ were determined in serum by ELISA (Vector-Best, Novosibirsk). Results of the study are presented as the median (Me) and quartile (Q1–Q3). The significance of differences between the features were determined using the Mann-Whitney test, the results were considered significant at $p \leq 0.05$.
Results: The level of IL-17 and IL-2 in serum was higher In the group of examinees with presence of antibodies specific to *H. pylori* than in the group without specific antibodies (1.18 (0–4.64); 2.46 (0–9.78) pg/ml and 0.96 (0–2.65); 0.2 (0–0.48) pg/ml, respectively. In the group with the presence of specific antibodies the level of IFN-γ was 16.4 (11.6–26.1) pg/ml, which was lower than in the group without specific antibodies (23.0 (17.8–26.6) pg/ml).
Conclusion: Thus, patients with *H. pylori*-infected, which have asymptomatic carrier state, there is an increase of IL-17, IL-2 and INF-γ serum. Detailed studies of the dynamic changes in the level of cytokines that regulate the differentiation of immunocompetent cells may be important in the development of the technology of early diagnosis of disease associated with *H. pylori*.

P06 Pathology and Pathophysiology

Abstract no.: P06.01

HELICOBACTER PYLORI, DECREASED PEPSINOGEN AND ATROPHIC GASTRITIS ARE NOT ASSOCIATED WITH BARRETTS ESOPHAGUS AND EROSIVE ESOPHAGITIS

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Introduction: *Helicobacter pylori* infection has been suggested to protect against erosive esophagitis (ERD) and Barrett's esophagus (BE). An explanation represents the development of corpus pre-dominant and/or atrophic gastritis in the natural course of *H. pylori* infection with a decrease in gastric acid secretion.
Aim and Methods: We assessed whether *H. pylori* infection, decreased serum pepsinogen levels as a marker for gastric atrophy and different forms of gastritis are associated with the occurrence of BE and ERD. We reviewed prospectively collected data of 332 patients that underwent gastroduodenoscopy. *H. pylori* status was determined by serology and serum pepsinogen I were measured in fasting state.
Results: In *H. pylori* infected patients (n = 101; 30.4%), the overall prevalence of ERD (20.8%) was comparable to non-infected patients (25.5%) ($p = 0.215$) and the same accounted for BE (7.9% vs. 11.7%) ($p = 0.214$). *H. pylori* was not associated with an increased risk for both ERD (OR = 0.76, 95% CI: 0.43–1.35) and BE (OR = 0.65, 95% CI: 0.28–1.49). The histological proof of IM and/or gastric atrophy did not show an association to neither ERD (OR = 0.61, 95% CI: 0.28–1.49) or BE (OR = 0.73, 95% CI: 0.32–1.67). The same accounted for different forms of gastritis. No association was seen between a decreased pepsinogen I and ERD (OR = 0.75, 95% CI: 0.37–1.54) and BE (OR = 0.82, 95% CI: 0.31–2.22).
Conclusion: *H. pylori* infection does not show any association to the occurrence of ERD and BE. Furthermore, different types of gastric inflammation and a hypoacid gastric function do not influence the development of ERD and BE.

Abstract no.: P06.02

DIFFERENT PATTERN OF INFLAMMATORY AND ATROPHIC CHANGES IN THE GREATER AND LESSER CURVATURE OF THE GASTRIC MUCOSA

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Background: The extent of inflammation and atrophy of different regions of the stomach in patients with chronic gastritis have been addressed only in few studies.The aim of our study was to analyze the inflammatory, atrophic, metaplastic changes and *H. pylori* colonization in the greater and lesser curvature of the antrum and corpus mucosa.Patients and methods. 423 patients undergoing upper endoscopy were enrolled in the study. Five biopsy samples was available (two samples from the greater and lesser curvatures of antral mucosa, one from the mucosa of the lesser curvature of incisura angularis, and two from the anterior and posterior walls of the corpus. Three expert gastrointestinal pathologists graded biopsy specimens according to the updated Sydney classification. Giemsa and immunohistochemical staining was used for the detection of *H. pylori*.Results. Obtained results showed that the acute and chronic inflammatory changes were more prominent in the corpus lesser curvature compared to corpus greater curvature ($p = 0.01$ and $p = 0.0001$, respectively). In addition, the extent and degree of atrophy and intestinal metaplasia (IM) was more prominent in corpus lesser curvature compared to greater curvature ($p = 0.002$ and $p = 0.0065$, respectively). Furthermore, *H. pylori* tend to be more frequently found in the corpus lesser curvature compared to greater curvature. Furthermore, differences between the inflammatory, atrophic, metaplastic changes and *H. pylori* colonization was observed in the antrum greater and lesser curvature.Conclusion. The findings confirm that random biopsy specimens have to be obtained both: from lesser and greater curvature to achieve better reliability.

Abstract no.: P06.03

SHOULD WE INITIATE ERADICATION THERAPY IN ACUTE GASTRIC MUCOSAL LESIONS?

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Background: Acute gastric mucosal lesions (AGML) is a relatively rare disease characterized by acute hemorrhagic gastritis, acute erosive gastritis, acute gastric ulcer, and combination of these. It is well known that there were many reports of AGML caused by acute *Helicobacter pylori* (Hp) infection at the time of endoscopic procedure in 1990's. But now, we usually deal with chronic gastritis derived from chronic infection of Hp because of the spread of an endoscope washing machine.
Method: We encountered seven cases of AGML diagnosed by endoscopy between December 2010 and May 2013. We studied clinical presentation and the ratio of positive test results in various diagnostic methods for Hp infection, consisting of urea breath testing, rapid urease testing, microscopy, culture and immunostaining.
Result: We confirmed Hp infection in six cases, and they were suspected of acute Hp infection based on the presence of regular arrangement of collecting venules in body of stomach. Using the serum antibody method at the onset, five of the cases tested negative. Once case was positive, but antibody value rose with time. Urea breath testing, rapid urease testing, microscopy, culture and immunostaining all demonstrated a proportion of false negatives, but feces antigen testing, implemented in the five cases, gave positive results in all cases. Where progress was monitored without eradication therapy, in two cases subjective symptoms were exacerbated, and one case demonstrated transition to persistent infection.
Conclusion: Most of AGML occur as a result of initial Hp infection. Eradication therapy should be carried out at an early stage of AGML.

Abstract no.: P06.04

RECOVERY OF SERUM PEPSINOGEN AFTER ERADICATION OF *HELICOBACTER PYLORI* IN SUBJECTS WITH PEPTIC ULCER: 10-YEAR FOLLOW-UP STUDY

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Background: There have been few reports about long-term follow-up data of serum pepsinogen (PG) after eradication of *Helicobacter pylori* (*H. pylori*).
Aim: To evaluate long-term gastric condition after *H. pylori* eradication by determination of serum PG levels.
Methods: Twenty-two gastric and duodenal ulcer patients (GU group n = 11, DU group n = 11) received yearly endoscopy and blood sampling for ten years after successful eradication. PG levels were determined using Chemiluminescent magnetic particle immunoassay (CLIA) and were compared between GU and DU groups at every year after eradication.
Results: There were no significant differences in the mean PG I and PG II values at baseline before eradication, and the mean PG I/PG II ratio in GU group was lower than that in DU group, significantly (3.65 ± 0.63 in GU group and 5.34 ± 1.43 in DU group). After eradication, the PG levels significantly changed at the first year, and there were no changes after the second year in both groups. The PG I/PG II ratio in DU group maintained high levels than that in GU group for ten years.
Conclusion: Gastric PG recovers within one year after *H. pylori* eradication depending on the mucosal atrophy before eradication.

Abstract no.: P06.05

ASSESSMENT OF POLYMORPHISM AT POSITION C421A OF ABCG2 GENE IN THE GROUP OF PATIENTS WITH PEPTIC ULCER

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Peptic ulcer is common disease with severe complications. Risk factors of peptic ulcer diseases development may include, among others: chronic use of non-steroidal anti-inflammatory drugs (NSAIDs), improper diet, smoking or alcohol consumption but primarily *Helicobacter pylori* infection.

BCRP protein is the *ABCG2* gene product. It is physiologically located in kidney, hepatic, ovaries and digestive tract. BCRP transports many substrates including toxins from cells into extracellular environment. It may therefore act as protective role.
One of the most frequent polymorphism of *ABCG2* gene is single nucleotide polymorphism (SNP) at position C421A. This SNP is connected with change of activity of *ABCG2* protein product what may result in accumulation of toxins in cells and may increase risk of peptic ulcer development.
The aim of the study was genotyping at position C421A of *ABCB1* gene in biopsy sample of stomach mucosa from patients with peptic ulcer and comparison the frequency of obtained genotypes distribution with control group.
Investigated group: 55 biopsy samples of stomach mucosa collected during gastroscopy
Control group: peripheral blood taken from 65 blood donors
Methods: urease test, DNA Isolation, PCR-RFLP
Investigated group on basis of results of rapid urease test was divided into to two subgropus patients infetcted and uninfected with *Helicobacter pylori*.
Preliminary study showed that in all control group and investigated group only CC genotype of SNP C421A occurred.

P07 Preneoplastic and Neoplastic Diseases

Abstract no.: P07.01

FICE DIAGNOSTIC ACCURACY FOR GASTRIC MUCOSAL ATROPHY PER BIOPSY AND PER PATIENT

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Background/Aims: Patients with chronic atrophic gastritis (AG) or intestinal metaplasia (IM) should be considered to be at higher risk for gastric adenocarcinoma. This study aimed to evaluate the correlation between endoscopic (flexible spectral imaging color enhancement (FICE) system) and histological findings of AG.
Methods: We included 191 consecutive patients (male 28%, average 62, range 50–87) from January 2013 to April 2014 aged over 50 undergoing FICE (gastroscope EG-590WR) endoscopy at Digestive diseases centre GASTRO. Targeted biopsies were obtained at the locations of visually suspected lesions. If no changes were determined by FICE, random biopsies were performed in antrum, incisura and corpus according to Sydney-Houston protocol. Histology assessment was performed according to the updated Sydney System. OLGA system was used and individuals classified accordingly.
Results: For the antrum the sensitivity, specificity, LR+ and LR- of endoscopic AG diagnosis per specimen were 40.24%, 68%, 1.26 and 0.88 and for the corpus: 46.3%, 90.36%, 4.8 and 0.59 respectively.
The sensitivity, specificity, LR+ and LR- of endoscopic AG diagnosis per patient (vs OLGA III/IV) were 82.35%, 78.57%, 3.84 and 0.22 respectively.
The overall prevalence of endoscopically and histologically diagnosed AG cases were 60% and 91% (65% OLGA I).
Conclusions: FICE endoscopy yielded favourable results in the endoscopic diagnosis of advanced stages of AG (OLGA III/IV) and this is very practical and easy way to use in a daily clinical practice for unselected patients.

Abstract no.: P07.02

THE MICRORNA PROFILE OF PRECURSOR LESIONS OF GASTRIC CANCER OBTAINED BY DEEP SEQUENCING

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Background: *Helicobacter pylori* leads to a high rate of morbidity and mortality from peptic ulcers and gastric cancer. Gastric cancer develops via a sequence of precursor lesions: atrophic gastritis, intestinal metaplasia, and dysplasia. Markers to classify the risk of precursor lesions are lacking. MicroRNAs (miRNA), a class of short non-coding RNAs that regulate gene expression, have been proposed as biomarkers.
Aim: To determine the miRNA profile in *H. pylori*-infected patients with precursor lesions of gastric cancer.
Methods: We used histology to classify 62 infected patients into *H. pylori*-positive without precursor lesions (n = 15) and *H. pylori*-positive or *H. pylori* -negative with precursor lesions (metaplasia or atrophy, n = 47). *H. pylori* status was determined by rapid urease test, urea breath test, and histology; additional antral biopsies were collected for miRNA sequencing. Total RNA was isolated from two pooled biopsies and prepared for sequencing using the TruSeq-SmallRNA Sample Prep Kit. Libraries were sequenced on an Illumina HiScanSQ system. Single-end reads were mapped and analysed using sRNAbench and R-edgeR.
Results: We found 375 miRNA species in more than ten reads in all 62 libraries. In patients with precursor lesions, 20 miRNAs were deregulated (six upregulated and 14 downregulated) by more than twofold compared to *H. pylori*-infected patients without precursor lesions (FDR<0.05).
Conclusions: The panel of deregulated miRNAs is being validated in an independent group of patients by qPCR. After evaluation for diagnostic accuracy, this miRNA panel may be useful for molecular classification of precursor lesions of gastric cancer.

Abstract no.: P07.03

FEASIBILITY OF ENDOSCOPIC SUBMUCOSAL DISSECTION WITH PLANNED ENDOSCOPIC SUBMUCOSAL DISSECTION WITH SNARING FOR GASTRIC ADENOMA COMPARED WITH STANDARD ENDOSCOPIC SUBMUCOSAL DISSECTION

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Aim: Planned Endoscopic Submucosal Dissection with Snaring (ESD-S) is thought to shorten operating time spent on submucosal dissection, but may lead to uncertainty of en bloc resection or to a possible increase in tumor-positive margins. The purpose of the present study is to investigate the feasibility of ESD-S as a planned procedure for gastric adenoma.
Methods: The medical records of 99 patients who underwent ESD-S or ESD for gastric adenoma between May 2011 and May 2012 were retrospectively reviewed. We analyzed the differences between the ESD-S and the ESD groups, focusing on rates of en bloc resection and pathologic complete resection, mean operation time, and complications.
Results: The mean operation time was significantly lower in the ESD-S group than in the ESD group (19.9 ± 11.2 vs 33.8 ± 19.9, $p = 0.012$). Cases with an operation time under 30 minutes were more frequent in the ESD-S group (88.9% vs. 48.1%, odds ratio = 8.615, 95% confidence interval = 2.949 – 25.168). There were no significant differences in en bloc resection, histologic complete resection, or complication rates between the two groups.
Conclusion: ESD-S has a time advantage over ESD with a comparable compete resection rate. ESD-S can be considered a planned method for available early gastric adenoma.

Abstract no.: P07.04

MANAGEMENT OF SUSPICIOUS MUCOSA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA IN BIOPSIED GASTRIC SPECIMEN OF SCREENING UPPER ENDOSCOPY

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Background/Aims: It is often difficult to differentiate gastric mucosa-associated lymphoid tissue (MALT) lymphoma from follicular gastritis. However, it is not well known how to manage those suspicious MALT lymphoma cases. This study aimed to elucidate the clinical course and management strategy of suspicious gastric MALT lymphoma detected by screening upper endoscopy with biopsy.
Methods: Between October 2003 and May 2013, consecutive subjects who were diagnosed as suspicious gastric MALT lymphoma by screening upper endoscopy in a health checkup program were retrospectively enrolled. Suspicious MALT lymphoma was defined as WHO/Wotherspoon score 3 or 4 in pathologic evaluation of gastric biopsy tissue.
Results: During the study period, a total of 101 103 subjects received 207 114 screening upper endoscopy. Among them, suspicious gastric MALT lymphoma was found in 76 subjects, all of whom were positive for *Helicobacter pylori* (*H. pylori*) infection. Excluding 16 subjects who were initially lost to follow-up, 60 subjects were enrolled, and gastric MALT lymphoma was confirmed in eight subjects (13.3%): three patients were initially diagnosed by using immunohistochemistry; two developed MALT lymphoma among eight patients without *H. pylori* eradication; one developed MALT lymphoma among four patients who failed *H. pylori* eradication; and two developed MALT lymphoma with *H. pylori* reinfection among 48 patients who were successful in *H. pylori* eradication. By contrast, there was no case developing MALT lymphoma among 46 patients in whom *H. pylori* was eradicated without reinfection.
Conclusions: Gastric lesions suspicious for MALT lymphoma with *H. pylori* infection may be managed with *H. pylori* eradication.

Abstract no.: P07.05

SUBSEQUENT MALIGNANCIES AFTER ERADICATION THERAPY FOR *HELICOBACTER PYLORI*

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Objective: To investigate the incidence of subsequent malignancies in patients who had purchased the needed combinations of 2–3 antimicrobials and an

acid-suppressing drug, required to cure *Helicobacter pylori* infection. Such combinations are rarely ordered for other indications.

Based on data from the national prescription registry and Finnish Cancer Registry,a cohort of 217 555 subjects (120 345 women and 97 210 men), who had purchased the specific combinations of drugs for eradication therapy in 1994–2004, was identified. The incidence of malignancies – from the purchase of the drugs until November 2013 (2 427 487 person years at risk) was analysed.

Results: A total of 29 243 malignancies were identified. In both genders, the high SIRs of stomach, pancreas, colon, (12- to 6-fold the national background level) and several other common malignancies (2- to 4-fold) for the first six months after the drug purchase, fell rapidly, but those of gastric non-cardia, colorectal, lung and prostate cancers remained elevated for up to five years of follow-up. The only SIRs below the population rates were seen first after that; for gastric cancers in men 81 intestinal non-cardia cancers (0.78, 95% CI: 0.62–0.97), while elevated SIRs were found for lung, liver, prostate and diffuse non-cardia cancers in men and lung cancers and non-Hodgkin lymphomas in women. The SIRs of other malignancies were then at unity.

Conclusions: Due to significantly elevated incidence of several common malignancies in *H. pylori* infected patients and similar non-specific symptomatology associated with these diseases, it seems indicated to investigate patients receiving eradication therapy for simultanous malignancies.

Abstract no.: P07.06

This abstract has been withdrawn.

Abstract no.: P07.07

ARE ALL PATIENTS WITH HISTOLOGICAL DIAGNOSIS OF ATROPHIC GASTRITIS REALLY AT RISK OF DEVELOPING GASTRIC CANCER? ASSESSMENT OF GASTRIC ACID PRODUCTION BY CORRELATION BETWEEN MAXIMAL ACID OUTPUT AND PEPSINOGEN I

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Chronic atropic gastritis results in loss of parietal cell mass which manifests itself in reduced or absent gastric acid secretion. Increase in gastric pH may permits colonization of the stomach by bacteria. Serum pepsinogens are regarded as alternative, non-invasive, but reliable gastric secretory parameters, potential screening tools to detect patients at risk of developing gastric cancer.

Aim: To assess the usefulness of serum biomarkers in evaluating gastric cancer risk.

Material and methods: A total of 42 subjects (18 male) were included in the study, aged between 41 and 71 years (mean: 53.7 years) and diagnosed with histologically confirmed AG (22 autoimmune). Fasting levels of pepsinogen I (sPGI), pepsinogen II and gastrin17 were measured as well as maximal acid output (MAO). Resulting data was statistically evaluated.

Results: Patients were subdivided in groups with achlorhydria (64.3%) and normal gastric function according to MAO values. Statistically significant differences were found between these groups regarding both pepsinogen and gastrin 17 levels. Significant correlation was found between sPGI and MAO (Spearman r = 0.782). A ROC curve identified the best sPGI cut-off point of 30 μg/L for the diagnosis of achlorhydria with a sensitivity of 100% (95% CI: 87.11–100), specificity of 93.33% (CI: 67.98–98.89) and negative predictive value of 100% (CI: 76.66–100).

Conclusions: There is a correlation between sPGI and MAO. Not all patients with histological diagnosis of AG suffer from achlorhydria. These patients can be identified using sPGI and may be eligible for serological follow-up instead of upper GI endoscopy.

Abstract no.: P07.08

REVERSAL OF ENDOSCOPIC GASTRIC ATROPHY DURING LONG TERM FOLLOW UP AFTER *H. PYLORI* ERADICATION

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Background: Recent studies have indicated that the eradication of *H. pylori* improves the histological gastric atrophy. However, there are no reports on the long-term observation of endoscopic changes of gastric atrophy and its expansion after eradication of *H. pylori*. We investigated the long-term effect of *H. pylori* eradication on the gastric mucosal atrophy assessed by endoscopy.

Methods: Thirty-eight patients who underwent gastroscopy every 1–3 years after eradication of *H. pylori* from1998 to 2003 were retrospectively studied. Gastric mucosal atrophy was endoscopically assessed according to the Kimura-Takemoto classification system and scored from 0 to 6 corresponding to C-0 (no atrophy), C-I, C-II, C-III, O-I, O-II, and O-III of the system, respectively. Endoscopic atrophy before eradication were also graded into mild (1–2), moderate (3–4) and severe atrophy (5–6). Follow up periods were divided to pre-eradication, the early (1–5 years after eradication), middle (6–9 years), and late (10–15 years) periods. Successive changes in scores for endoscopic atrophy before and after eradication were analyzed.

Results: The median of atrophy score was significantly decreased from 3.5 to 3.5 (early: $p = 0.023$), 3(middle: $p < 0.001$) and 2 (late: $p < 0.001$) after eradication. When stratified based on the atrophic grades before eradication therapy, decreases in the score for atrophy was more evident in the mild atrophy group in comparison with the intermediate and severe groups.

Conclusion: Eradication of *H. pylori* infection improved gastric mucosal atrophy assessed by endoscopy during the long-term period, especially in the patients with mild atrophy.

Abstract no.: P07.09

GASTRIC EPITHELIAL DYSPLASIA: CHARACTERIZATION AND LONG-TERM FOLLOW UP RESULTS ACCORDING TO MORPHOLOGICAL CATEGORIZATION

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Background: Gastric epithelial dysplasia (GED) can be morphologically categorized into adenomatous, foveolar and hybrid types, but there are few studies on the clinical and endoscopic characteristics in the types of GED, especially assessing their correlation with long term outcome after endoscopic resection. The aims of this study were to elucidate clinicopathological characteristics and long term follow-up results according to each type of GEDs after endoscopic resection.

Methods: From January 2008 to December 2009, 357 patients who underwent endoscopic resection of GEDs at Pusan National University Hospital were studied. Retrospectively, comparisons of clinicopathological characteristics including endoscopic findings between the types of GED were assessed and long term follow-up data (synchronous, metachronous lesions and detection of gastric cancer after endoscopic resection) were evaluated.

Results: Adenomatous type made up the biggest proportion, 46.8%, followed by 28.9% for foveolar type. The foveolar type of GEDs was significantly more likely than adenomatous type to show endoscopically located on antrum, flat/depressed lesion, reddish in color, and to reveal histopathologically high grade dysplasia. In the long term follow-up results, adenomatous type was of synchronous lesions significantly more often than foveolar and hybrid type ($p = 0.013$). However, there were no significant differences among the types in terms of the metachronous, and detection of gastric cancer during a median follow-up period of 41.1 months (range, 12–69.5 months) after endoscopic resection.

Conclusions: In our study of endoscopically resected GEDs, GEDs have different clinicopathological characteristics as well as long-term follow up results according to each subtype.

Abstract no.: P07.10

DIFFERENCE OF SERUM PEPSINOGEN LEVEL BETWEEN *H. PYLORI*-INFECTED AND NON-INFECTED CURRENT HEALTHY JAPANESE ADULTS

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Background and Aim: Serum pepsinogens (PGs) have been used to identify patients with atrophic gastritis. Usually, atrophic gastritis is considered positive when both PG I level of <70 ng/mL and PG I/II ratio of <3.0 were obtained. However, this cut-off was defined in 1980s when prevalence of *H. pylori* was higher. The aim of this study was to examine whether the current cut-off is appropriate for current population.
Methods: Of 639 healthy adults who received health survey in 2012 were studied. We measured stool antigen, serum antibody, and serum level of PGs. Subjects were considered as infected when stool antigen test and/or serum antibody were positive. Subjects were defined as never-infected when stool antigen was negative, antibody titer was less than limit and without history of eradication. Subjects taking PPI and with previous gastric surgery were excluded.
Results: Level of PG I was <70 ng/mL in most never-infected subjects. Level of PG I was significantly higher in infected patients than never-infected subjects aged less than 60 ($p < 0.05$) while it was significantly lower in infected patients aged over than 70 ($p < 0.05$). Level of PG II was significantly lower in non-infected subjects in any generation ($p < 0.05$). PG I/II ratio was also significantly higher in non-infected subjects in any generation ($p < 0.05$).
Conclusions: PG I level of <70 ng/mL is not a useful cut-off for *H. pylori* non-infected subjects. Since the prevalence of *H. pylori* infection is decreasing, appropriate level of serum PGs should be established using current populations.

Abstract no.: P07.11

THE ROLE OF NON-INVASIVE ASSESSMENT OF THE SECRETORY FUNCTION OF THE GASTRIC MUCOSA IN DYSPEPSIA

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Introduction: Chronic atrophic gastritis (CAG) is precancerous condition, a risk factor for dysplasia and subsequent development of intestinal type gastric cancer (GC). Serum levels of PG-I (fundic mucosa), PG-II (chief cells,pyloric glands and proximal duodenal) and G-17 (G cells) reflect inflammation and atrophy of gastric mucosa.
Aims & Methods: The aim of this study was to evaluate, for the first time in our population, clinical significance of serum levels of PG-I, PG-II, PG-I/PG-II ratio and G-17 as serum markers of gastric atrophy. We have analyzed 73 patients (38 males; mean age 62) with dyspepsia, according to ROME III criteria. Oesophagogastroduodenoscopy was performed, between February and December 2011 in Clinical Center Bezanijska Kosa. At least two biopsies were taken from antrum, corpus and incisura angularis for histological analysis by using Updated Sydney System. Serum levels of PG-I, PG-II and G17 were assessed using ELISA test. Statistical analysis was done using SPSS 19.
Results: By the Roma III criteria for FD, 38 (52.1%) patients had epigastric pain syndrome, 35 (47.9%) patients suffered from postprandial distress syndrome. Corpus atrophy was histologically found in 3 (4.1%) patients and significantly correlated with PG-I levels lower than 25 ($r^2 = 0.4$, p 0.05); sensitivity 33.3% and specificity 18.5%. In precancerous condition, H.pylori infection was histologically found in 53.3%.
Conclusion: Serum levels of PG-I lower than 25 and PG-I/PG-II ratio lower than five can be used as markers of corpus gastric atrophy with high specificity. G17 levels were not useful in our population for prediction of antrum gastric atrophy.

Abstract no.: P07.12

IS SERUM ANTI-*HELICOBACTER PYLORI* IMMUNOGLOBULIN G TITER ASSOCIATED WITH ADVANCED COLORECTAL ADENOMA?

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Backgrounds and Aims: Recent studies have revealed the positive relationship between *Helicobacter pylori* (*H. pylori*) gastritis and colorectal adenoma. It has been suggested that serum anti-*H. pylori* (Hp) immunoglobulin G (IgG) titer may correlate with grades of gastric mucosal inflammation and mucosal *H. pylori* density. The aim of this study was to investigate whether serum anti-Hp IgG positivity is associated with colorectal adenoma and high anti-Hp IgG titer can predict advanced adenoma.
Methods: We retrospectively enrolled 460 patients who underwent screening colonoscopy and *H. pylori* IgG test from January 2013 to March 2014. Univariate and multivariate analyses were performed to identify whether serum anti-Hp IgG positivity is associated with colorectal adenoma. The mean values of anti-Hp IgG titer were calculated and compared.
Results: *H. pylori* seropositive group had more colorectal adenoma than seronegative group [110/280 (39.3%) *vs.* 41/180 (22.8%), $p = 0.0001$]. In multivariate analysis, *H. pylori* seropositivity [Odds ratio (OR), 1.82; 95% confidence interval (CI), 1.123~2.961; $p = 0.015$] as well as old age ($p = 0.0001$) and male gender ($p = 0.004$) was significantly associated with colorectal adenoma. The mean anti-Hp IgG titer of advanced adenoma was higher than non-advanced adenoma and non-adenoma (2.6 ± 1.66 vs 2.28 ± 1.73 vs 1.93 ± 1.68, $p = 0.008$, respectively). When the titer was classified as high titer group (>2.6) and low titer group (≤2.6), the prevalence of advanced adenoma was not significantly different between two groups [36/74 (48.6%) vs. 30/77 (39%), $p = 0.23$].
Conclusions: Serum anti-Hp IgG positivity was an independent predictor of colorectal adenoma, although, high anti-Hp IgG titer could not predict advanced adenoma.

Abstract no.: P07.13

HOW CAN WE MANAGE INCIDENTAL SMALL SUBEPITHELIAL MASS IN UPPER GASTROINTESTINAL TRACT?

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Objectives: Subepithelial mass is a relatively common finding in upper gastrointestinal endoscopy. The aim of this study was to evaluate the natural course of asymptomatic subepithelial masses in upper gastrointestinal tract and analyze the risk factors of the subepithelial masses increasing in size.
Methods: From 2004 to 2011, 2126 subepithelial masses in upper gastrointestinal tract were detected, and 935 were followed up using endoscopy.
Results: The lesion size at initial endoscopy was 8.7 mm (range 1–100 mm). During a mean follow-up of 35.2 ± 21.2 month (range 6–96 month), 903 subepithelial masses (96.6%) were showed no interval change, 32 lesions (3.4%) were increased at least 25% in diameter with mean increment 5.0 ± 4.0 mm (range 1–15 mm). The risk of increasing subepithelial mass was significant in overlying mucosal changes (hyperemia, erosion, or ulcer) (OR = 8.22, 95% CI 1.48–45.70) and hard consistency (OR = 10.348, 95% CI 1.10–97.35). We evaluated the increasing velocity as size increment divided by follow-up years. The increasing velocity was faster (0.44 ± 2.12 mm/year, range 0.00–15.00 mm/year) for large lesions (≥2 cm) than small lesions (0.07 ± 0.38 mm/year, range 0.00–5.14 mm/year for <2 cm) ($p < 0.001$).
Conclusions: Most of the small subepithelial masses were showed no interval change during 8 year follow-up period. Regular follow-up with endoscopy may be considered in small (<2 cm) subepithelial masses with intact overlying mucosa.

Abstract no.: P07.14

GASTRIC PRECANCEROUS LESIONS IN *HELICOBACTER PYLORI* POSITIVE ALGERIAN POPULATION: WHAT PREVALENCE?

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Aims: The aim of this study was to evaluate precancerous gastric lesions prevalence in *Helicobacter pylori* positive patients.
Methods: From 2002 to 2012, 1068 patients have been enrolled in a multicenter prospective study (mean age: 38.3 years, Male: 389,UD: 139 DNU: 929). An upper endoscopy with 5 per- endoscopic biopsies (antrum:2, fundus: 2, Incisura: 1) was performed in all patients. The diagnosis of Hp infection was attested by the positivity of 4 tests: UBT, TRU, Histology and culture. Histological analy-

sis, using gastritis Sydney system and OLGA score, was performed in co- observation between 3 and 5 pathologists.
Results: The respective rates of antral and corpus atrophy were 74.3% 50.4%.Hp infection was noted in 92% of cases. Antral and corpus atrophy were severe in respectively 4.4% and 1.5% of cases. Risk of severe atrophy was slightly higher in case of Hp infection (RR = 1.2). Metaplasia prevalence was 14%. Mild to moderate dysplasia was observed in 25 patients (1.8%). Its topography was antral in the majority of cases (antrum: 18, corpus:3, antrum and corpus: 4). Dysplasia rates in older(>60 years) and younger(<60 years) subjects were equivalent(2.3% vs 2.4%, $p = 0.96$).
Conclusion: In our study, the risk of severe atrophy was slightly higher in the case of Hp infection. Metaplasia was uncommon while dysplasia was rare. These data make Algeria as a country with low risk of gastric adenocarcinoma despite its high Hp infection prevalence.

Abstract no.: P07.15

FACTORS FOR SUCCESSFUL ENDOSCOPIC SUBMUCOSAL DISSECTION IN PYLORIC NEOPLASMS: LOCATION AND DIRECTION

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Background and Aims: The anatomical features of pylorus can adversly affect the assessment of tumor margin and ESD procedure, consequently piecemeal resection and complication rates in pyloric neoplasms is higher compared with other sites of gastric neoplasms.
Methods: A total 110 pyloric adenomas and early cancers resected by ESD at our hospital from January 2007 to May 2013 were reviewed retrospectively. The location type was defined according to the presence of duodenal invasion: pylorus lesion (distal margin of the tumor was located <0.5 cm from pyloric ring); pylorus with duodenal extension lesion (any invasion to duodenal side beyond pyloric channel). A clock-face orientation with the endoscope (with the lesser curve of the stomach in contiguity with the 12 o'clock orientation of pylorus) was used to characterize directional distribution.
Results: The rates of complete resection differed significantly in relation to location (pylorus vs pylorus with duodenal extension, 79% vs 58%, respectivley; $p = 0.039$) and directional distribution (upper hemisphere vs lower hemisphere, 67% vs 90%, respectively; $p = 0.009$) and tumor size (<10 mm vs ≥10 mm, 84% vs 67%, respectively; $p = 0.049$) and circumference extent of pylorus mucosal resection (<1/2 vs ≥1/2, 92% vs 62%, respectively; $p = 0.001$). There were no significant complications. On multivariate analysis, tumor location and hemisphere distribution and circumferential extent of resection were significantly relevant for complete resection.
Conclusion: ESD of pyloric neoplasms is effective and feasible, but endoscopists require advanced technique and more experience,if located in pylorus with duodenal extension, upper hemisphere and large circumferential extent of resection (≥1/2) because of low complete resection rates.

Abstract no.: P07.16

SERUM ANTIBODIES AGAINST SECRETED PEPTIDYL PROLYL CIS, TRANS-ISOMERASE HP0175 OF *HELICOBACTER PYLORI* CORRELATE WITH THE INTENSITY OF GASTRITIS

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Background: Secreted peptidyl prolyl cis-, trans-isomerase, HP0175 activates tumor infiltrating lymphocytes through activation of pro-inflammatory cytokines, which are thought to be responsible for pre-cancerous gastric histopathologic changes. This study has evaluated the association between HP0175-specific antibody response and grade of gastric inflammation.
Methods: Hp0175 gene was PCR-amplified, cloned and expressed in T-vector and pET28a vectors, respectively. The identity of rHP0175 was evaluated by gene sequencing and immune reactivity against Hp-positive sera. Purification of His tagged rHP0175 was performed using affinity chromatography on a Ni2 + -NTA column. Serum reactivity against rHp0175, in 52 Hp-infected patients and its association with the grade of inflammation (I,II,III,IV) was evaluated.
Results: A 900 bp DNA fragment encoding 35 kDa Hp0175 protein was amplified. The identity of the recombinant fragment was confirmed by gene sequencing (Genbank Accession No.: KF801473.1), which revealed 96% nucleotide homogeneity with published sequences in the GenBank. The 35 kDa protein was visualized by SDS-PAGE and its immunogenicity was confirmed by pooled Hp-positive sera. Serologic reactivity to rHp0175 was associated with the grade of inflammation ($p = 0.016$) and resulted in enhanced (OR = 11.2, 95% CI = 1.751–71.637, $p = 0.011$) risk of advanced grades (III & IV) of gastric inflammation.
Conclusion: Serologic reactivity to rHp0175 may be applicable as a non-invasive representation of the intensity of *H. pylori* associated gastric inflammation. However, larger sample sizes are required to validate this hypothesis.

Abstract no.: P07.17

RISK FACTORS OF DELAYED ULCER HEALING AFTER GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION

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Aim: The aim of this study is to clarify risk factors of delayed ulcer healing after gastric endoscopic submucosal dissection (ESD). Methods: We reviewed medical records of patients who had ESD for gastric high-grade adenoma or early gastric cancer between January 2005 and February 2012. Delayed ulcer healing was defined as sustaining unhealed iatrogenic ulcer at 3 months after the ESD. To find potential risk factors we reviewed following parameters: age, sex, comorbidity that might influence mucosal healing, history of peptic ulcer, laboratory abnormalities, antiplatelet or NSAID usage, size of the specimen, location and histologic type of lesion, *Helicobacter pylori* status, and hot biopsy. Results: Out of the total 1680 patients enrolled, 95 had delayed ulcer healing. In multivariate analysis, diabetes (OR 1.743; 95% CI: 1.017–2.989, $p = 0.043$), coagulation abnormality (OR 3.195; 95% CI: 1.535–6.650, $p = 0.002$), specimen size greater than 4 cm (OR 2.999; 95% CI 1.603–5.611, $p = 0.001$), and hot biopsy (OR 7.149; 95% CI 1.738–29.411, $p = 0.006$) were revealed to be independent risk factors of delayed ulcer healing. Meanwhile, persistent *Helicobacter pylori* infection was not shown to be related to the delayed ulcer healing. Conclusion: Patients those who had ESD for large gastric lesions and massive hemostasis, especially those with diabetes or coagulation abnormalities, tend to have delayed healing of iatrogenic ulcer. For such patients initial dosage increment of PPI or addition of other anti-ulcer agents after ESD should be considered.

Abstract no.: P07.18

CLINICAL AND ENDOSCOPIC FEATURES OF METASTATIC TUMORS IN THE STOMACH

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Background: The presence of metastasis in the stomach is rare. The aim of this study was to describe and analyze the clinical outcomes and endoscopic findings of metastatic cancers in the stomach.
Methods: We reviewed the clinicopathological aspects of patients with gastric metastases from solid organ tumors. Thirty-seven cases were identified, and we evaluated the histology, initial presentation, imaging findings, lesion locations, treatment courses, and overall patient survival.
Results: Among all 37 cases with metastases to the stomach, endoscopic findings showed that solitary lesions (n = 23, 62.2%) were more presented than multiple lesions (n = 14, 37.8%) and submucosal tumor-like tumor was the most common appearance (n = 12, 32.4%). Malignant melanoma was the most frequent tumor that metastasized to the stomach (n = 10, 27.0%). Twelve patients (32.4%) any received treatments after the diagnosis of gastric metastasis. Thirty-three patients died (89.2%) and the median survival period from the diagnosis of gastric metastasis was 3.0 months (interquartile range [IQR] = 1.0–11.0 months). Patients with solitary lesions and patients who had received any treatments survived longer after the diagnosis of metastatic cancer than patients with multiple lesions (7.0 months vs 2.0 months, respectively; $p = 0.047$) and patients who did not any receive any treatments (11.0 months vs 2.0 months, respectively; $p < 0.001$).
Conclusion: Proper treatment with careful consideration about the characteristics of the primary tumors can increase the survival period in patients with metastatic tumor to the stomach, especially in cases with solitary metastatic lesions in endoscopic findings.

Abstract no.: P07.19

RISK FACTORS AND CORRELATION OF IMMEDIATE, EARLY DELAYED AND LATE DELAYED BLEEDING ASSOCIATED WITH ENDOSCOPIC RESECTION FOR GASTRIC MUCOSAL LESIONS

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Background and Aims: Bleeding is a major complication after endoscopic resection (ER) for gastric mucosal lesions. We aimed to determine the risk factors and correlation of post-ER bleeding according to three periods after procedure.
Patients and methods: Between March 2009 and December 2010, a total of 670 lesions in 610 patients who underwent ER were retrospectively enrolled. We classified into three types according to the bleeding time; immediate (IB), early delayed (EDB) and late delayed bleeding (LDB). We analyzed risk factors in each type focused on the patient's baseline characteristics, procedure related factors and the correlation between the occurrence of each bleeding type.
Results: Post-ER bleeding occurred in 408 events in 610 patients, IB in 302, EDB in 88 and LDB in 18. In multivariate analysis, histologic finding (carcinoma) and resection time were significant predictors of IB ($p < 0.001$). Of 302 events with IB, 13.9% showed EDB. 2.4% with EDB and 4.6% without EDB showed LDB. Of 368 events without IB, 12.5% showed EDB, which was similar to the IB group. 2.2% with EDB and 1.24% without EDB showed LDB. IB revealed higher risk of EDB ($p < 0.001$) and LDB ($p < 0.001$), while EDB event did not show increased risk of LDB ($p = 0.997$).
Conclusion: Histologic finding (carcinoma), resection time increased the risk of bleeding related to ER. IB increased the risk of EDB and LDB. Patients with IB should be performed second look endoscopy, and when necessary, proper hemostasis is required to reduce LDB.

Abstract no.: P07.20

This abstract has been withdrawn.

P08 Oesophageal and Extradigestive Diseases

Abstract no.: P08.01

H. PYLORI AND CLINICAL COURSE OF PREGNANCY

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Aim: To evaluate the influence of *H. pylori* (HP) on clinical course of pregnancy.
Patients and Methods: The course of pregnancy was analyzed in 200 women divided into three groups: 1st – 100 women (mean age 32.1 years) with diseases associated with HP, 2nd – 50 women (mean age 28.8 years) with upper GI diseases HP negative, 3rd – 50 healthy pregnant women (mean age 26.1 years). HP was detected by 13C-urease breath test or by rapid urease test.
Results: Non developing pregnancy was registered in history of 28% of HP positive women vs. 6% HP negative ($p = 0.011$). Early pregnancy toxemia was more severe and lasted till 16 week of pregnancy in 1st group vs 11 week in 2nd group and 8 week in 3rd group. Vomiting as symptom of early pregnancy toxemia was detected in 42% cases in 1st group vs. 36% in 2nd group and 24% in 3rd group (p1-3 = 0.047). Anaemia was in 31% of women in 1st group vs. 24% in 2nd group and 18% in 3rd group. The level of Hb was significantly lower 9.2 ± 0.3 g/L (vs 10.4 ± 0.2 g/L ($p < 0.05$) in 2nd group and 11.6 ± 0.3 g/L ($p < 0.05$) in 3rd group), and its treatment was more difficult. Frequency of vaginal candidiasis was higher in 1st group. We found no difference in frequency of late pregnancy toxemia, in outcome of pregnancies.
Conclusion: HP is associated with frequency, severity and length of early pregnancy toxemia, frequency and severity of anaemia, and frequency of vaginal candidiasis.

Abstract no.: P08.02

THE RELATIONSHIP BETWEEN *H. PYLORI* INFECTION AND OSTEOPOROSIS IN JAPAN

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Background and Objective: H.pylori infection causes a chronic inflammation in the gastric mucosa. However, this local inflammation may result in extradigestive conditions, such as osteoporosis. However, there are no studies examining the relationship between H.pylori infection and osteoporosis in Asia. The aim of study is to investigate the relationship between H.pylori infection and osteoporosis in Japan.
Methods: This cross-sectional study was conducted among outpatients (>50 years) at our department between March 2008 and February 2014. Participants profiles for age, sex, body mass index (BMI), alcohol consumption, smoking, diabetes mellitus (type 2), hypertension, proton pump inhibitor, low dose aspirin, H.pylori infection status, dual-energy x-ray absorptiometry, vertebral x-rays, bone specific ALP (BAP), collagen type I cross-linked N telopeptide (NTX) and FSSG questionnaire were collected and upper gastrointestinal endoscopy for reflux esophagitis, hiatal hernia, peptic ulcer diseas (PUD) and endoscopic gastric mucosal atrophy (EGA) was performed. We divided the subjects into osteoporosis and non-osteoporosis groups and investigated risk factors of osteoporosis using bivariate and multivariate analysis.
Results: Of the eligible 200 study subjects (mean age 63.1 ± 8.8 years; 95 male), 41 cases (20.5%; 8 male) were osteoporosis. Bivariate analysis showed that advanced age, female gender, lower BMI, alcohol consumption, smoking, H.pylori positive, BAP, PUD, and EGA were related with osteoporosis. Multivariate analysis showed that advanced age (OR 1.13; 95%CI 1.07–1.20), female gender (OR 4.77; 95%CI 1.78–12.77), lower BMI (OR 0.79; 95%CI 0.68–0.92), H.pylori positive (OR 5.33; 95%CI 1.73–16.42), and the presence of PUD (OR 4.98; 95%CI 1.51–16.45) were related with osteoporosis.
Conclusions: *H.pylori* infection may be a risk factor of osteoporosis in Japan.

Abstract no.: P08.03

ATROPHIC GASTRITIS AS A RISK CONDITION FOR THE DEVELOPMENT OF POSTMENOPAUSAL OSTEOPOROSIS

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Background and Aim: Atrophic gastritis is associated with a low intragastric acidity. Under this condition, calcium salts are minimally dissolved and, subsequently, may not be properly and effectively absorbed. Therefore, atrophic gastritis may increase the risk of osteoporosis but their clinical relationship has been poorly studied so far. The aim of this study is to evaluate the relationship between the presence of atrophic gastritis and osteoporosis.
Methods: We retrospectively reviewed medical records of the subjects who underwent esophagogastroduodenoscopy and bone densitrometry by dual energy X-ray absorption for routine health check-up. The presence of atrophic gastritis was determined by two experienced endoscopists according to the Kimura classification. Results: A total of 1184 subjects (aged 30–92 years, mean age 58.9 years) were reviewed in this study. Among 672 female subjects, 34(5.1%) of them were diagnosed with osteoporosis. All female subjects with osteoporosis were postmenopausal. Among them, 30(88.2%) had atrophic gastritis. On the other hand, among 512 male subjects, 6(1.2%) of them were diagnosed with osteoporosis. All male subjects with osteoporosis had atrophic gastritis. After adjustment for risk factors, including old age, body mass index, physical activity, and smoking, atrophic gastritis was a significant risk factor only for the postmenopausal osteoporosis ($p = 0.000$, Adjusted odds ratio 20.64, 95% Confidence interval 4.77–89.23)
Conclusions: Atrophic gastritis seems to be a risk condition for postmenopausal osteoporosis. Therefore, consideration of absorption problems due to atrophic gastritis and low intragastric acidity might be helpful for the management of postmenopausal osteoporosis.

Abstract no.: P08.04

GUT AND GASTRIC MICROBIOTA CHARACTERISTICS IN RELATION TO *HELICOBACTER PYLORI* STATUS IN A PEDIATRIC POPULATION

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The aim of this study was compare gastric and gut microbiome among children according to *H. pylori* status.
Gastric biopsies and rectal swabs were obtained during upper endoscopy from 28 symtomatic children. For gastric biopsies we performed: Rapid Urease Test, Culture, and qPCR (specific 16S *H. pylori* rRNA in LightCycler®480). DNA was extracted from biopsy using Ultraclean Tissue & Cells DNA Isolation Kit (MoBio) and from rectal swab using PowerLyzer PowerSoil DNA Isolation Kit (MoBio). A 16s rRNA library was prepared from each specimen and sequenced with MISeq Ilumina. Alfa and beta diversity were studied using QIIME software. Four gastric biopsies were excluded from analysis.
True positive *H. pylori* patient was considered when 3 test were positive (n = 7), probable positive when only two were positive (n = 3), possible positive when one test was positive (n = 2) and true negative when all tests were negative (n = 16).

Table: *H. pylori* sequences in gastric biopsies according to tha *H. pylori* status

H. pylori status	*H. pylori* sequences
True positive	66.1%
Probable positive	15.7%
Posible positive or true negative	0.8%

Gastric bacterial communities were significantly different from intestinal communities independently of *H. pylori* status.
Patients with *H. pylori* colonization have lower alpha diversity in the gastric microbiome than patients without *H. pylori* colonization.The distribution of rela-

tive taxa was identical in children with or without *H. pylori*. We did not identified *H. pylori* sequences in the gut microbiome of the true positive *H. pylori* children.

Abstract no.: P08.05

H. PYLORI ERADICATION DOES NOT AFFECT THE GERD COURSE IN ELDERLY PATIENTS: THE RESULTS OF A 5-YEAR PROSPECTIVE STUDY

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Aim: To assess the dynamics of non-erosive reflux disease (NERD), erosive reflux disease (ERD) and Barrett's esophagus (BE) in elderly patients with eradication of *H. pylori* infection during the 5-year prospective study.

Methods: We performed a prospective five-year observation of 469 elderly GERD patients (300 females, 169 males, median age 78.1 years). Of these, in 290 patients at beginning of the study was conducted successful eradication of infection *H. pylori* (group A). 179 patients during the observation period had an infection *H. pylori* (group B). GERD was diagnosed on the basis of the Montreal Consensus (Vakil N et al., 2006). The presence of erosive esophagitis was classified based on the Los Angeles classification (Lundell LR et al., 1999). During the five-year follow-up clinical examination and endoscopy of the esophagus performed twice a year. Morphological examinations of the esophagus to determine BE were done in the beginning and the end of study.

Results: In the group A after 5 years of observation NERD frequency decreased from 46.9% to 41.7% ($p = 0.2$), ERD frequency increased from 44.5% to 49.0% ($p = 0.3$), BE frequency increased from 8.6% to 9.3% ($p = 0.9$). In the group B NERD frequency decreased from 48.0% to 42.5% ($p = 0.3$), ERD frequency increased from 44.7% to 49.2% ($p = 0.5$), BE frequency increased from 7.3% to 8.4% ($p = 0.8$).

Conclusion: We found that eradication therapy *H. pylori* had no significant effect on the dynamics of NERD, ERD and BE for a five-year observation period.

Abstract no.: P08.06

ASSOCIATION BETWEEN SERUM LEVEL OF PEPSINOGENS AND PROTEIN INTAKE IN HEALTHY JAPANESE ADULTS INFECTED WITH *H. PYLORI*

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Background and Aim: Level of serum pepsinogens (PGs) has been used to assess the condition of the gastric mucosa. Although PGs are precursors of pepsin, the association of serum PGs and protein intake has not been fully examined. The aim of this study was to examine the association of serum level of PGs to protein intake in patients with *H. pylori* infection.

Methods: Of 639 healthy adults who received health survey in May 2012 were studied. We measured *H. pylori* stool antigen, titer of serum antibody to *H. pylori* and serum level of PG I and II. Subjects who were taking PPI and had previous history of gastric surgery were excluded. Protein intake during the previous month was calculated using a brief-type comprehensive self-administered diet history questionnaire (BDHQ). Regression coefficient between level of PGs and protein intake was calculated.

Results: In patients with *H. pylori* infection, protein intake was smaller than that of non-infected subjects <50 years old. In contrast, larger protein intake was observed in infected patients over than 60 years old. There was a significant positive correlation between PG I/II ratio and protein intake in female patients infected with *H. pylori* (r: 0.006, $p < 0.05$). However, no significant correlation was found in subjects without *H. pylori* infection.

Conclusions: The results would suggest that progress of glandular atrophy (lower PG I) and severer mucosal inflammation (higher PG II) were associated with lower protein intake in female patients with *H. pylori* infection.

Abstract no.: P08.07

THE INFLUENCE OF *HELICOBACTER PYLORI* ON LIPID METABOLISM IN PATIENTS WITH CORONARY HEART DISEASE

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In recent years, much attention is devoted to extraintestinal manifestations of *Helicobacter pylori* (H.P.). A studying of a possible connection between *H. pylori* infection and coronary heart disease still stays on a first place.

Objective: To investigate the condition of lipid metabolism in patients with coronary heart disease, infected with H.P.

All patients were divided into two groups. To the first group included 32 patients (20 men and 12 women) infected with H.P.

To the second group included 31 patients (18 men and 13 women) without the H.P. infection.

In patients in both groups was studied a level of total cholesterol, triglycerides, high-density lipoprotein (HDL), low density lipoprotein (LDL) and the level of C-reactive protein.

At the time of the examination, patients did not take any lipid-lowering drug therapy during the last 3 months.

In patients of the I group total cholesterol level was significantly higher ($p < 0.01$) comparing to group II patients (6.67 ± 0.29 mmol/L vs 5.56 ± 0.23 mmol/L).

The level of C-reactive protein was significantly increased in patients of the I group ($p < 0.05$) comparing with the patients of the II group (1.96 ± 0.22 vs 1.19 ± 0.32).

It was no differences ($p > 0.05$) of the levels of triglycerides and HDL in the patients of I group (1.82 ± 0.21 mmol/L, 1.43 ± 0.09 mmol/L) and the II group (1.49 ± 0.2 mmol/L, 1.46 ± 0.11 mmol/L).

There is observed deeper metabolic disorders of lipids and the increased level of C-reactive protein in patients with coronary heart disease infected with H.P. comparing with non infected patients.

Abstract no.: P08.08

THE ASSOCIATION BETWEEN EADICATION OF *HELICOBACTER PYLORI* AND INCREASING OF PLATELET COUNT IN PATIENTS WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA

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Background and Aim: We investigate the association between eradication of *H.pylori* and increase of platelet count in patients with idiopathic thrombocytopenic purpura.

Methods: This was a retrospective study created from chart review for patients who diagnosed by idiopathic thrombocytopenic purpura. All patients (n = 42) were assessed for *H.pylori* infection by use of a urea breath test. The patients of positive result by urea breath test were received 7-days standard triple therapy to eradication of *H.pylori* infection. At the 6 months after eradication therapy, idiopathic thrombocytopenic purpura patients with a platelet count recovery of greater than 100×10^9 L^{-1} were defined as thrombocytopenic purpura improved group.

Result: Fourteen patients were identified as idiopathic thrombocytopenic purpura improved group; twenty-eight patients were considered ITP non-improved group. The eradication rates of *H.pylori* were better in ITP improved group (8/8, 100%) than ITP non-improved group (6/14, 42.9%). Platelet counts improved by more than 100×10^9 L^{-1} in 14 (63.6%) of the 22 patients cured of *H.pylori* infection, 6 (30%) of the 20 patients *H.pylori*-negative patients experienced the same improvement ($p = 0.018$). The eradication of *H.pylori* increased the odds ratio (OR) of the increasing platelet count in ITP patients (OR: 5.35, 95% CI: 1.09–26.33, $p = 0.039$)

Conclusion: Eradication of *H.pylori* in idiopathic thrombocytopenic purpura patients resulted in improvement of disease activity. The eradication of *H.pylori* increased the odds ratio (OR) of the increasing platelet count in ITP patients (OR: 5.35, 95% CI: 1.09–26.33, $p = 0.039$).

Abstract no.: P08.09

PROTECTIVE ROLE OF *HELICOBACTER PYLORI* INFECTION AGAINST SEVERE REFLUX ESOPHAGITIS

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Introduction: Possible interaction between Helicobacter Pylori (H.P.) infection and Gastroesophageal Reflux Diesease (GERD), is derived from data showing that as the prevalence of HP infection decreased in the West, the prevalence of GERD and esophagitis increased.
Methods: The aim was to investigate the prevalence of H.P. infection among patients with reflux esophagitis. A retrospective analysis was conducted on all patients with reflux esophagitis (n = 361), during a 3-year-period (2011–2013). Seventy asymptomatic patients that were submitted to esophagogastroduodenoscopy because of iron deficiency anemia, without clinical or endoscopic evidence of esophagitis, were used as controls. H.P. status was confirmed through histology or breath test.
Results: Esophagitis was graded into four groups, according to L.A. classification: grade A (168 patients), B (94 patients), C (68 patients), and D (31 patients). The prevalence of H.P. infection was lower (but not significantly) in patients with esophagitis compared to controls (51.24% vs 55.7%, NS). After separating patients into two groups, according to esophagitis severity (mild esophagitis: grade A+B, severe esophagitis: grade C+D), H.P. prevalence was the following: 57.25% of patients with mild esophagitis (NS compared to controls), and 35.35% of patients with severe esophagitis ($p < 0.05$ compared to controls).
Conclusion: A remarkably lower prevalence of H.P. infection was noted in patients with severe esophagitis (grade C + D), but not in patients with mild esophagitis (grade A + B). This supports a possible protective role of the H.P. infection against the development of severe esophagitis.

Abstract no.: P08.10

HUMAN ANTIBODY RESPONSE AGAINST *HELICOBACTER PYLORI* CAGA MAY PLAY A ROLE IN ATHEROSCLEROTIC-RELATED DISEASES THROUGH MOLECULAR MIMICRY MECHANISMS

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Clinical and experimental evidence indicates a significant association between CagA seropositivity and vascular diseases. This correlation could be linked to molecular mimicry mechanisms by which anti-CagA antibodies may recognize human endothelial antigens, therefore interfering with their function. In our work, three N-terminal His6-tagged recombinant fragments of CagA protein were obtained in the native form through application of SUMO fusion expression system. Protein CagA-fr.1 (65 kDa) represents the most conserved N-terminal part of the cytotoxin. Fragment CagA-fr.2 (44 kDa) corresponds to the central conserved region of CagA whereas CagA-fr.3 (39 kDa) represents the highly variable C-terminal region. By means of Ni $^{++}$chromatographic purification, high levels of purity (90%) and yield (10 mg/L of culture) of recombinant CagA fragments were achieved. To evaluate patients' immune response against CagA, ELISA were performed using CagAfr.2 as target antigen since it is found to be the most immunogenic fragment. Five sera from patients with unstable plaques showed an antibody titer against CagA higher than Hp positive sera from as many patients with stable vascular disease. A Selected serum with the highest anti CagA titer has then been used for immunoblot assays against self-antigens deriving from coronary plaques total proteins extract showing a reactivity against a 50 kDa antigen yet to be identified. Our preliminary results show that the study of human antibody response against *Helicobacter pylori* CagA can greatly contribute to the understanding of the role played by this important virulence factor in the bacterium–host interplay that may lead to autoimmune responses.

Abstract no.: P08.11

TUBEROUS SCLEROSIS AND *HELICOBACTER PYLORI* INFECTION: MORE THAN A SIMPLE ASSOCIATION?

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Helicobacter pylori is involved in exacerbation of many digestive and extradigestive diseases, including several chronic neurological conditions like multiple sclerosis, Parkinson and Alzheimer's diseases.
In this paper we report the case of a young Patient affected by Tuberous Sclerosis, a rare genetic neurocutaneous disorder, with a recent precipitation of seizure episodes with associated gastrointestinal symptoms (dyspepsia, epigastric pain, belching and regurgitation). Biochemical, radiological and endoscopic tests showed a gastris associated to *Helicobacter pylori* (Hp) infection. The patient underwent to classical triple therapy with subsequent eradication of H,p confirmed by Urea Breath Test.
After *Helicobacter pylori* eradication, gastrointestinal symptoms disappeared with a rapid improvement of epileptic manifestations, which lowered in number and severity.
Considering the significant neurological improvement after *Helicobacter pylori* eradication, it could be hypothesized a specific role for Hp infection and/or gastric symptoms in triggering seizures of patients affected by Tuberous Sclerosis.
In fact, there is a possible pathophysiologic link between *Helicobacter pylori* and Tuberous Sclerosis: both conditions are associated to a significant alteration of mTOR-MAPK pathway with abnormal cell growth and cancer transformation.
It could be hypothesized that *Helicobacter pylori* infection can be a stimulating factor in the growth of brain lesions during Tuberous Sclerosis, through deregulation of mTOR-MAPK pathway. Hence, the Hp eradication could promote the stability of cerebral lesions in tuberous sclerosis.
In conclusion, it would be convenient search for Hp infection in Tuberous Sclerosis patients with "neurological instability", however more studies are needed to better characterize this possible connection and to provide evidence-based clinical indication.

Abstract no.: P08.12

CYTOPROTECTIVE EFFECT OF BISMUTH-BASED QUADRUPLE THERAPY IN THE PATIENTS WITH ATROPHY AND JOINT HYPERMOBILITY SYNDROME

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Background: Violation of functional activity of connective tissue cellular elements in the patients with joint hypermobility syndrome (JHS) promotes change of reparative processes and defective collagen formation, can be a significant pathogenetic mechanism of gastric mucosa atrophy (GMA).
Aim: Assessed the dynamics of gastric mucosa morphological changes of patients with JHS on the background of bismuth-based quadruple therapy.
Methods: Within the time period from Feb 2011 to Apr 2014 74 patients with JHS and 58 patients without JHS were examined by serology and 13C-Urea breath test. Biopsies were evaluated according to the Sydney classification, Houston viewing on the modified visual-analog scale (OLGA scale).
Results: There was a significant predominance of atrophy (45.9% vs. 12.1%, $p < 0.05$) and metaplasia (25.7% vs. 5.2%, $p < 0.05$) precisely in the group of patients with JHS. There was found the reduction of gastric atrophy on the background of eradication with bismuth-based quadruple therapy in the patients with JHS in comparison with the patients without JHS.
Conclusions: Significant prevalence of atrophic changes of the patients with JHS proves the role of connective tissue disorders in the development and progression of GMA changes along with Hp persistence. The large percentage of cases of undetermined atrophy among the patients with JHS requiring differential diagnostics exactly on the background of cytoprotective effect of bismuth.

P09 Paediatric Issues

Abstract no.: P09.01

EFFECT OF *HELICOBACTER PYLORI* INFECTION ON GHRELIN, OBESTATIN, AND LEPTIN SERUM LEVELS IN MEXICAN CHILDREN WITH NORMAL BODY MASS INDEX AND OVERWEIGHT

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H. pylori (Hp) infection in adult has been demonstrated to affect the gastric and systemic levels of ghrelin, obestatin, and leptin, as well as producing post-eradication changes in the levels of these hormones. Ghrelin, obestatin, and leptin play a vital role in the regulation of appetite and satiety, thereby affecting homeostatic energy that is translated into body weight. Aim. To assess the relationship between Hp infection and ghrelin, obestatin, and leptin serum levels in children with normal BMI and overweight. Metodology. In 178 children were determined the status of Hp (C14Urea Breath Test) and anthropometric measurements. The children were categorized as Hp+ normal BMI, n = 60 and overweight BMI, n = 27, Hp- normal BMI, n = 60 and overweight BMI, n = 31 and fasting serum were obtained. These hormones were determined by specific commercial ELISA kits, Human Ghrelin Total, Human Leptin, and Human Obestatin. Results. The serum levels were comparatively analyzed among all groups by ANOVA and the levels of the three hormones were found to be lower in Hp+ groups than in the Hp- groups independently of BMI (p 0.001). There was no correlation between the serum levels of ghrelin and obestatin with BMI. Nevertheless, there was a significant correlation in the case of leptin (p 0.0001). Conclusion. Hp infection was associated with a reduction in the serum levels of grelin, obestatin, and leptin in mexican children. Hp infection, especially during childhood, may have influence on the nutritional status of the host through changes in serologic levels of these hormones.

Abstract no.: P09.02

HELICOBACTER PYLORI CAGA AS A DOMINANT ANTIGEN RECOGNIZED BY JAPANESE CHILD SERUM ANTIBODIES

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Serological diagnosis for *Helicobacter pylori* infection is established for adults, however, it has been problematic for Japanese children. We have found that the diagnostic performance of an enzyme immune assay (EIA) kit based on Japanese strain-derived high-molecular-weight cell-associated protein (JHM-CAP kit) was much better than that based on U.S. strain-derived high-molecular-weight cell-associated protein (HM-CAP kit), although the performances of the two kits for adult populations were not much different. Such a clear difference between the two kits for diagnosis of *H. pylori* infection in Japanese children was shown to be attributed mainly to the 100-kDa antigen protein contained only in JHM-CAP. The aim of this study is to determine the antigenic properties unique to Japanese strains of *H. pylori* by proteomic analysis.

We performed two-dimensional gel electrophoresis using lysate of *H. pylori* strain CPY2052 followed by immunoblot with IgG antibodies in sera from 22 *H. pylori*-positive and 2 *H. pylori*-negative Japanese children. Antigenic proteins were identified by LC-MS/MS analysis. In total, 24 proteins were identified as candidate antigens. Among these, CagA was the most reactive antigen that was recognized by all the *H. pylori*-positive sera even from children under the age of 3 years. By using a new array chip method, two epitopes were identified in the middle region of CagA that was unique to East Asian strains. These results indicated importance of the local CagA antigens for serodiagnosis of *H. pylori* infection in children.

Abstract no.: P09.03

THYROGASTRIC AUTOIMMUNITY IN CHILDREN

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Background: An association between autoimmune thyroid disease (AITD) and atrophic body gastritis (ABG) has been evidenced in adults. Few studies have analyzed this association in children. Gastropanel represents a non-invasive instrument indicating morphological status of gastric mucosa through measurement of serum pepsinogens (PGI, PGII), gastrin-17(G-17) and H.Pylori antibodies.

Objective: Aim was to determine the existence of an association between AITD and ABG in children, the possibility of detecting children at risk through Gastropanel, and predictiveness of its markers.

Population and methods: We evaluated gastropanel markers, parietal cell antibodies (PCA), thyroid function and aoutoantibodies (TPO, TG) in 20 children with AITD (group 1), in affected family members (group 2) and in controls (group 3).

Results: TSH, fT4, TPO and TG levels were not correlated with gastropanel markers in the group as a whole. Higher percentage of pathological levels of PGI, PGII, G-17 and PCA were demonstrated in group 1 compared to controls. The comparison between mean values evidenced that PGI, PGII and PCA levels in group 1 were situated between those in groups 2 and 3.

Conclusions: Correlation between age and PCA and PGI levels confirmed the importance of age in onset of autoimmune gastritis. Discrepancy between PGI and G-17 levels was evidenced in children with AITD, with a higher percentage of hypergastrinemia compared to lower levels of PGI, allowing us to hypothesize that gastric autoimmunity tends to appear later and that the first manifestation may be modest hypergastrinemia. Our results indicate that children with AITD should be evaluated for gastric autoimmunity.

Abstract no.: P09.04

A HIGH PREVALENCE OF *HELICOBACTER PYLORI* INFECTION AMONG CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Background: Epidemiologic data suggests a protective effect of HP (*Helicobacter pylori*) infection against disease with an autoimmune component. Preliminary evidence in adults suggests that patients with IBD (Inflammatory Bowel Disease) are less frequently infected with HP. We aimed to examine the prevalence of HP infection among Israeli children with IBD compared to non- IBD children.

Methods: Rates of HP infection were compared between newly diagnosed IBD patients and two control groups. Group A- children who underwent upper and lower endoscopy for suspected IBD and the diagnosis was deferred. Group B – children diagnosed with celiac disease who had a biopsy specimen taken from the stomach. Age at diagnosis and gender were documented.

Results: Data from 334 endocopic and pathologic reports were collected. 112 patients were diagnosed with IBD, 96 with crohn's disease, 12 with Ulcerative Colitis and 4 with IBD-U (undefined). 78/112 (69.6%) children with IBD, mean age 13.5 ± 3.3 were HP positive. 49/82 (59.7%) children without IBD, mean age 13.7 ± 3.1 were HP positive. 94/140(67.1%) children with Celiac disease, mean age 8 ± 5.0 were HP positive. The prevalence of HP infection was exceptionally high in all three groups. There was no difference in the mean age of children with and without HP infection (11.34 vs 11.14 years). The mean age of the celiac patients was lower.

Conclusions: The prevalence of HP infection is high among children with newly diagnosed IBD in Israel. This data is in contrast to previous studies in adults demonstrating an inverse association between HP and IBD.

Abstract no.: P09.05

NUTRITIONAL STATUS OF CHILDREN ADMITTED IN A DIGESTIVE ENDOSCOPY UNIT, ASSESSED BY INTERNATIONAL GROWTH CHARTS

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Our country is in a phase of nutritional transition and doesn't have updated its growth charts.

To assess the agreement between the New World Health Organization (WHO,2007) and the Center of Disease Control (CDC,2000) growth charts and to evaluate the relationship between H pylori and poor nutritional status in symptomatic children.

This was an observational study of 314 consecutive symptomatic children (213 girls, mean age 9.5 years) requiring first esophagogastroduodenoscopy in our units during the past 3 years. All patients were evaluated for z-score of: weight/age (WAZ), stature/age (HAZ) and body mass index/age (BMI/A) in each of the two references. Active H pylori infection was documented by urease test and histological examination in 144 (45.86%) of 314 symptomatic children. For statistical analysis were used: EPI INFO 3.5.3 (CDC,2000), ANTHRO PLUS (WHO,2007), SPSS 18.0.

The patients nutritional status showed a significant Pearson correlation (>0.5), between CDC and WHO for all the three z-score indexes used, respectively 0.962 for WAZ, 0.949 for BMI/A and 0.921 for HAZ. Z-score of BMI/A estimated by WHO criteria was more efficient than CDC for the diagnosis of both ends of the spectrum of poor nutritional status: undernutrition (wasting 44 cases/14.01%; risk to underweight 49 cases/15.6% versus underweight 84 cases/26.75%) and overnutrition, respectively 31 (9.86%) versus 28 (8.92%).

H pylori infection was associated with both ends of the spectrum of poor nutritional status. The use of WHO references seems to be more efficient for the children's nutritional screening at the hospital admission in particular in developing countries.

Abstract no.: P09.06

UPPER, BUT NOT LOWER, RECURRENT ABDOMINAL PAIN IS ASSOCIATED WITH CHRONIC *HELICOBACTER PYLORI* INFECTION IN SIBERIAN ADOLESCENTS WITHOUT GASTRODUODENAL EROSIVE-ULCER LESIONS

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Many worldwide studies have shown no relation between recurrent abdominal pain (RAP) and chronic *Helicobacter pylori* (Hp) infection in schoolchildren; however, there are some limitations for final conclusion. First, most studies did not make any separation for upper and low RAP; second, data regarding this relation are mostly available for regions with low Hp prevalence; third, the age should be take into consideration as the important factor.

Aim: To investigate the relation between RAP and Hp presence according to RAP localization and frequency in Siberian adolescent.

Methods: Of 100 adolescents with RAP complaints (aged 11-17, boys/girls ratio – 44/56), referred to a pediatric gastroenterology center (Krasnoyarsk, Russia), were screened by Questionnaire on Pediatric Gastrointestinal Symptoms Rome III Version (QPGS-RIII) and tested to Hp (Hp antigen ELISA monoclonal test in stool, Immundiagnostik, Germany). No adolescents had erosions or ulcer according to upper endoscopy.

Results: Progressive positive association was detected between upper RAP frequency and Hp presence (Table 1). A subgroup of adolescents with lower RAP did not exhibit any relation between RAP frequency and Hp infection.

Conclusion: We suppose that RAP diagnostics in adolescents with high frequency upper abdomen pain pattern in region with high infection prevalence should include Hp testing. However, eradication usefulness in this subgroup of patient requires futher investigation.

Table 1. Hp positivity percentages in adolescents with different RAP localization and frequency

	ANSWERS			
QPGS-RIII QUESTIONS	Never or 1 to 3 times a month 1	Once a week 2	Several times a week or every day 3	p (two-tailed exact Fisher test)
In the last 2 months, how often did you have pain or an uncomfortable feeling *in the upper abdomen above the belly button*?	34% (16/47)	46% (11/24)	59% (17/29)	p1-3 = 0.036
In the last 2 months, how often did you have a belly ache or pain *in the area around or below the belly button*?	47% (35/75)	20% (2/10)	43% (6/15)	No statistical differences ($p > 0.05$)

Abstract no.: P09.07

SPECTRUM OF RADIOGRAPHIC FINDINGS IN CHILDREN WITH *HELICOBACTER PYLORI* INFECTION

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Introduction: Nowadays there is lack of information about radiographic criteria of H.pylori gastrointestinal (GI) disease in dyspeptic pediatric population.

The aim: to determine the most important samples of radiographic appearance of gastroduodenal mucosa detecting H.pylori infection in childhood.

Methods: We revealed 139 cases of antral CG and PU diagnosed using double contrast upper gastrointestinal examinations in the archive of the Radiology department of our hospital (2001–2011 years). All the findings were stratified to determine any helpful radiological features of H.pylori presence. The diagnosis of H.pylori infection was based on upper GI endoscopy with gastric histology. In the statistical analysis Chi-square test was used.

Results: All the patients suffered from chronic dyspepsia. Seventy seven patients (55.4%) (mean 12.7 + 1.1 years old, 36 male) were H.pylori positive. The rest of 62 patients (44.6%) (mean 10.3 + 1.4 years old, 39 male) were H.pylori negative (control group).

Enlarged gastric folds in the antrum and corpus were detected in 29 patients with H.pylori (37.66%) and in 11 control subjects (17.74%) ($p = 0.008$). Antral chronic erosions (defined as "complete" by endoscopy and histology) were found in 18(23.38%) H.pylori-positive patients vs 2(3.23%) who were H.pylori-negative ($p = 0.0009$). Antral nodularity was found in H.pylori-positive children only (9 patients, 11.69%) ($p = 0.007$). DU (proven by endoscopy) was diagnosed in 12 patients with H.pylori (15.58%) vs 1 patient from the control group (1.61%), ($p = 0.006$).

Conclusion: The presence of enlarged gastric folds, chronic antral erosions, nodularity, and duodenal ulceration, detected by radiographic examination, can suggest *H. pylori*-associated origin of gastroduodenal lesions in childhood.

Abstract no.: P09.08

CURRENT STATUS AND CLINICAL IMPACT OF PEDIATRIC ENDOSCOPY IN KOREA

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Background: In pediatrics, endoscopic examination has become a common procedure for the evaluation of gastrointestinal presentations. However, there are limited data on the pediatric endoscopy in Korea. We aimed to analyze the current status and clinical impacts of endoscopic examination in children and adolescents.

Methods: We retrospectively reviewed the medical records of outpatients who visited pediatric department at St. Vincent hospital and St. Paul hospital, the Catholic University of Korea. Patients under 18 years of age who underwent endoscopy were included.

Result: In a total 724 of 330 350 patients (0.2%), endoscopic examination (554 esophago-gastroduodenoscopys (EGDs), 170 colonoscopys) was performed between January 2007 and December 2011. In EGD, abdominal pain was the most frequent presentation (64.1%). The most common diagnosis was gastritis (53.2%), followed by reflux esophagitis (17.7%). The frequency of peptic ulcer disease was 12.8%. The episode of upper gastrointestinal bleeding was happened in 8.2% (45 / 554 patients). Twelve patients (26.7%) were duodenal ulcer and 10 (22.2%) were gastric ulcer. In total 71 patients with peptic ulcer disease, state of *Helicobacter pylori* (*H. pylori*) infection could be identified in 59 patients. The positive tests for *H. pylori* was observed in 21 patients (21/59, 35.6%). After the procedure, the rate of change in management change was 61.9%.

Conclusions: Most frequent symptom leading to pediatric endoscopic examination was abdominal pain. In pediatrics, endoscopic examination was useful for the choice of therapeutic strategy.

P10 Diagnosis

Abstract no.: P10.01

SCREENING OF *HELICOBACTER PYLORI* INFECTION USING STOOL ANTIGEN TEST FOR YOUNG ADULTS IN A JAPANESE POPULATION WITH HIGH INCIDENCE OF GASTRIC CANCER

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Background and Aim: In Japan, requirement of prior endoscopy has been a limitation to diagnose *H. pylori* infection in people who cannot visit medical institutes in day time. In 2012, two local governments, locate in north Japan with high incidence of gastric cancer, started a survey of *H. pylori* infection for people younger than 40 years old.
Methods: Subjects collect stool samples by themselves using the collection device and send them by post. *H. pylori* stool antigen is measured by a monoclonal antibody based stool antigen test (SAT) using EIA. Infected patients undergo endoscopy and receive measurement of serum pepsinogens. After informing the individual risk of gastric cancer based on endoscopic findings and pepsinogens, infected patients received eradication therapy. The results of eradication are also examined by SAT. Cost for patients is covered by the local governments.
Results: Until March 2014, 1883 subjects received SAT and 289 were tested positive. Positivity of SAT was 11.3%, 11.5%, 17.5% and 19.3% in patients aged 20–25, 26–30, 31–35 and 36–40, respectively. 226 of 289 patients received measurement of PGs and endoscopy. Positivity of serological atrophic gastritis was 0%, 20.0%, 28.0% and 33.0% in patients aged 20–25, 26–30, 31–35 and 36–40, respectively. Eradication rate of the first and second line therapies was 62.7% and 97.5%.
Conclusion: Screening using SAT is useful to identify patients with *H. pylori* in young adults. This strategy would be important for the prevention of gastric cancer, as well as inhibition of spread of infection to children in this area.

Abstract no.: P10.02

REAL-TIME PCR FOR DIAGNOSING *HELICOBACTER PYLORI* AND DETERMINING CLARITHROMYCIN SUSCEPTIBILITY IN PATIENT WITH DYSPEPSIA

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Aim: Clarithromycin resistance in *H. pylori* infection is a major factor leading to treatment failure. Therefore, there is a need to assess to predict an optimal and useful method to detect *H.pylori* and determine clarithromycin resistance where the clarithromycin resistance rate is high.
Methods: Two-hundred-thirty-four patients with dyspepsia (65 M, 169 F; mean age 43.8 ± 14.0 years) admitted to Gastroenterology Outpatient Clinic at Dokuz Eylül University Hospital were examined for rapid-urease-test, histopathology, culture and RT-PCR as a widely used molecular test. The diagnosis of *H. pylori* infection was defined as positive for at least two positive results of RUT-histopathology-culture. Four-hundred-sixty-eight antrum and corpus biopsy specimens were cultured and E-test was used. Biopsy DNAs were extracted and Real-time PCR method was performed.
Results: *H. pylori* positivity was found in 164(70.1%) patients; 114(69.5%) of them were culture positive, 157(95.7%) of them were positive by real-time PCR (sensitivity 95.7% and specificity 70%). 114 culture positive patients, 76 (66.7%) were clarithromycin-susceptible, 18 (15.8%) were -resistant and 20 (17.5%) were -susceptible and resistant by real-time PCR. A2142/2143G was the most common mutation associated with clarithromycin resistance in our study. Clarithromycin resistance was 28.0% and 33.3% by E-test and real-time PCR in both antrum and corpus biopsy specimens.
Conclusion: Because of its high sensitivity and specificity, real-time PCR is a effective tool to determine *H.pylori* positivity and clarithromycin susceptibility in the region where the resistance rates are high and antimicrobial susceptibility testing is required.
Key words: *Helicobacter pylori,* Real-time PCR, clarithromycin resistance

Abstract no.: P10.03

EVALUATION OF STOOL REAL-TIME PCR TO DETECT *HELICOBACTER PYLORI* AND TO DETERMINE CLARITHROMYCIN SUSCEPTIBILITY IN COMPARISON WITH BIOPSY REAL-TIME PCR IN PATIENTS WITH DYSPEPSIA

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Aim: To evaluate stool real-time PCR (RT-PCR) method to detect *H.pylori* and determine clarithromycin-resistance which is due to AàG transition at 2142/2143 positions and AàC transversion at 2142 position in 23S rRNA gene.
Methods: A-hundred-ninety-four patients with dyspepsia (54 M,140 F;mean age 45.3 ± 13.5 years) included in this study.*H.pylori* positivity was defined as positive at least two positive results of RUT, histopathology and culture. RT-PCR method was performed to extracted DNAs (QIAGEN) of 194 stool and 388 antrum and corpus biopsy specimens.All stool specimens were also studied with 10^{-1} dilutions simultaneously for good results to avoid inhibitors in feces for RT-PCR.E-test was used to assess clarithromycin susceptibility for isolated *H.pylori* strains.
Results: A-hundred-thirthy-five (69.6%) patients were *H.pylori* positive according to at least two positivity.*H.pylori* positivity by biopsy and stool RT-PCR were 129(95.6%) and 125(92.6%) in 135 patients.The sensitivity and specificity of biopsy and stool RT-PCR was 95.6%, 92.6% and 69.6%, 11.9% respectively ($\kappa = 0.690$, $\kappa = 0.056$).Evaluation of clarithromycin susceptibility;85(65.9%) and 108(86.4%) were clarithromycin-susceptible, 20(15.5%) and 4(3.2%) were –resistant, 24(18.6%) and 13(10.4%) were –susceptible and resistant by biopsy and stool RT-PCR, respectively.Resistance to clarithromycin was obtained 34.1%, 13.6% and 28.4% by biopsy and stool RT-PCR and E-test, respectively.The concordance between E-test and RT-PCR was 78.7% in biopsy and 71.6% in stool specimens.
Conclusion: Stool RT-PCR is highly sensitive and fast method for the detection of *H.pylori* and determination of clarithromycin susceptibility as a non-invasive method, although the specificity was found very low.In addition, different results between E-test and RT-PCR may be associated with different point mutations in the different positions/region of 23S rRNA which couldnot be detected by RT-PCR.

Abstract no.: P10.04

DIAGNOSTIC YIELDS OF PCR USING TISSUE SAMPLE FROM RAPID UREASE TEST KIT (CLO TEST) FOR THE DETECTION OF *HELICOBACTER PYLORI* IN PEPTIC ULCER BLEEDING

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Background: In patients with peptic ulcer bleeding (PUB), the prevalence rate of *Helicobacter pylori* infection may be underestimated. The causes for decreased diagnostic sensitivity of *H. pylori* test in PUB are still controversial. We aim to investigate the diagnostic yield of Polymerase Chain Reaction (PCR) to the detection of *H. pylori* in PUB.
Method: A consecutive series of patients who had PUB and admitted to the hospital between 2012 and 2013 were enrolled, and a total of 170 patients were analyzed. During the 2nd look endoscopy, two sets of gastric biopsy specimens were taken from the greater curvature of the mid-antrum and corpus for histology and CLO test. After interpretation of CLO test, the tissue samples from the kit were used, and dual-priming oligonucleotide-based multiplex PCR (DPO-PCR) was performed to the detection of *H. pylori* and antibiotic resistance. If the result was *H. pylori* -negative, re-biopsy specimens under endoscopy was taken after 4–8 weeks of initial examination.
Results: In PUB, the prevalence rate of *H. pylori* infection was 63.4% (104/164). At initial diagnostic sensitivities of histology, CLO test, and PCR test were 70.2% (73/104), 51.9% (54/104) and 92.3% (96/104), respectively ($p < 0.01$). The rate of clarithromycin resistance by using the 23S rRNA point mutation was 22.1% (23/104).
Conclusion: For diagnosis of *H. pylori* infection in PUB, DPO-PCR test with tissue sample from CLO test kit were the most sensitive test. Additionally, the information of clarithromycin resistance would be helpful for selection of the eradication regimens for *H. pylori.*

Abstract no.: P10.05

STABILITY OF $^{13}CO_2$ BREATH TESTS SAMPLES OVER TIME IN THE DIAGNOSIS OF *HELICOBACTER PYLORI*

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The accuracy and repeatability of breath test in the diagnosis of *Helicobacter pylori* (HP) infection is debatable. Although it has been shown that storage for long periods does not affect the analysis results, no data are available, on the effect of repetitive testing.

Our aim was to evaluate the repeatability of the analysis of the breath samples.

A total of 202 breath samples were collected in duplicates, before and after administration of 75 mg urea-^{13}C dissolved in 50 mL of orange juice and the results were expressed as delta $^{13}CO_2$ ($d^{13}CO_2$). The cut-off value was 3.5 parts per thousand. Each sample was analyzed in a mass spectrometer 7 days after collection and in intervals of 7 days for the duration of additional 3 weeks. The precision calculation was based on the comparison of the $d^{13}CO_2$ obtained in the three consecutive weeks following the first run to the $d^{13}CO_2$ obtained in the first run. The samples were stored at room temperature.

In the second run, 200 out of the 202 (99%) samples were tested positive for HP and the precision of the $d^{13}CO_2$ was 98.6%. In the third run, 197 out of the 202 (97.52%) samples tested positive and the precision was 99.2%. In the fourth and final run 196 out of the 202 (97%) samples tested positive and the precision was 96.7%.

We conclude that short term storage of 1 month, does not affect sample stability and the results of HP diagnosis for up to three consecutive repeats.

Abstract no.: P10.06

IDENTIFICATION OF VIABLE *H. PYLORI* CELLS IN FAECES BY DVC-FISH

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Helicobacter pylori detection in faecal samples is a more comfortable practice than invasive techniques, mainly in children. Nevertheless, culture and identification of this pathogen from stools is difficult and normally unsuccessful. Other techniques, such as PCR or *H. pylori* Stool Antigen (HpSA) are used. However, a positive result by these techniques does not involve pathogen viability.

Direct Viable Count combined with Fluorescent in situ Hybridization (DVC-FISH) has been successfully applied to identify viable *H. pylori* cells in water samples. The objective of this work was to assess the suitability of DVC-FISH technique to detect viable *H. pylori* cells in faecal samples.

Methods: Artificially *H. pylori* inoculated faeces and faecal samples from infected patients were analyzed directly and after enrichment by DVC-FISH, qPCR with VacA primers and culture techniques. For DVC analysis, sample was incubated in a specific broth supplemented with novobiocin prior to FISH analysis with a specific LNA-probe. *H. pylori* presumptive colonies on agar were identified by FISH and PCR.

Results: Viable *H. pylori* cells were detected by DVC-FISH in all samples from both inoculated and patients faeces. qPCR yielded positive results only in inoculated samples and without enrichment in all cases. Cultivable *H. pylori* was recovered from all inoculated samples and from only one clinical sample. Results demonstrate the presence of viable *H. pylori* in faecal samples from infected patients.

Conclusion: DVC-FISH technique by using LNA/DNA probes has the potential to be used as a specific and effective method for detection of viable *H. pylori* in stool samples.

Abstract no.: P10.07

THE DIAGNOSIS OF *H. PYLORI* IN TISSUE SECTIONS: AN INSTITUTIONAL QUALITY ASSURANCE REVIEW

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Background: Several staining methods are available for *H. pylori* (Hp) identification in tissue sections of chronic gastritis (CG), including the routine H&E method. Some reports suggest that ancillary stains are not always needed to establish the diagnosis of Hp infection and their added value when biopsies show minimal inflammation is not clear.

Aims: We performed a retrospective study to compare the usefulness of the H&E staining to widespread ancillary Giemsa method for the diagnosis of Hp in tissue sections.

Methods: We reviewed tissue sections from 370 consecutive patients at Laboratory of Histopathology, Alfa Institute of Gastroenterology, UFMG, Belo Horizonte, Brazil. Patients were divided in 3 groups according the inflammatory changes of the gastric mucosa, as follows: Group A, CG with patent inflammatory activity (n = 123); Group B, CG with mild inflammatory activity (n = 101), and Group C, gastric mucosa presenting normal morphology or minimal inflammatory changes (n = 146). All histological sections were thoroughly evaluated by 2 examiners.

Results: The identification of Hp by Giemsa and H&E were, respectively: Group A, 111 (90.2%) and 93 (75.6%) patients ($p < 0.01$); Group B, 43 (42.6%) and 29 (28.7%) patients ($p < 0.05$). Hp was not found in Group C.

Conclusions: The present results show that the widespread Giemsa method should be superior to H & E staining for histological identification of Hp in CG. The Hp can be seen easily by H&E method in majority of the patients studied; however, a significant number of infected patients can be overlooked regardless the degree of the inflammatory activity.

Abstract no.: P10.08

COMPARATIVE ANALYSIS OF EFFICACY OF NONINVASIVE AMMONIUM "HELIC-TEST" AND HISTOLOGICAL METHOD IN DIAGNOSTIC OF *HELICOBACTER PYLORI* INFECTION

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Background: A breath test with C13 urea is recommended as a one of the main methods for diagnostic of *Helicobacter pylori* infection. However, this method is not common in use in Russian gastroenterology practice. Therefore, we can use alternative noninvasive tests to diagnose *Helicobacter pylori* infection.

The Aim: To make an assessment of results of "Helic-test" in comparison with results of a histological method in diagnostic of *Helicobacter pylori* infection.

Materials and Methods: Of 171 patients (in 2008–2013) with dyspepsia were surveyed. By all patients for verification of *H. pylori* were made noninvasive ammonium "Helic-test" ("Association of medicine and analytics, St-Petersburg, Russia) and histologic test with two biopsies (one – from antrum and one- from body of stomach). The choice of a histological method as reference method was dictated by that, using this method, J.R. Warren and B.J. Marshall described existence of a helicoid bacterium in a mucous membrane of a stomach of patients with active chronic gastritis. Patients during two weeks before diagnostic did not take any medications, capable to change results of tests (inhibitors of a proton pomp, antibiotics, antacids, bismuth).

Results: The analysis of results in patients surveyed showed that coincidence of results of tests took place in 87.5% of cases. Sensitivity – 92%, specificity – 93%.

Conclusions: These results show the efficacy of breath ammonium test in comparison to histological method. Therefore, we can recommend this test for noninvasive diagnostic of *H. pylori* infection.

Abstract no.: P10.09

HELICOBACTER PYLORI IN NIGERIA

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Background: *Helicobacter pylori* is the causative agent of gastritis, ulcer and is a risk factor in the development of gastric cancer. The study is aimed at screening for *H. pylori* in Nigeria using different methods.

Methods: A total of 577 patients were screened for *H. pylori* by UBT, CLO, culture, histology and PCR.

Results: Out of a total of 577 patients screened from 2010 to 2013, 281 (48.7%) were UBT positive, 19 (3.3%) were not done, CLO was positive in 172 (29.8%), not done (2.1%). 119 (20.6%) were *H. pylori* positive from 69 patients. All isolates were confirmed *H. pylori* by PCR of 16S rRNA gene of *H. pylori*, while 88% were glmM positive. Endoscopic findings from 69 patients showed 30 (43.5%) had normal mucosa, 24 (34.8%) erosion, 20 (29%) oedema, 8 (11.6%) ulcer while 6 (8.7%) duodenitis. Cag A was present in 86% by PCR and 75% by western blotting. Of 354 biospies screened for histology, no cancer, ulcer or dysplasia was seen. 30% had MALT lymphoma, 7.1% had atrophy, 4.2% had metaplasia, while 40.7% had activity of inflammation of 2.

Discussion: *H. pylori* is still a problem in Nigeria although no gastric cancer case was reported in our study both by histology and endoscopic findings. In order to monitor resistance patterns culture is still paramount as there was a low prevalence by culture. Frequent power outages still affect accurate isolation and culture of *H. pylori* in Nigeria.

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Abstract no.: P10.10

EVALUATION OF EFFICIENCY OF HELIC AMMONIA BREATH TEST FOR DIAGNOSTICS OF *H. PYLORI* INFECTION IN STOMACH IN RHEUMATOID ARTHRITIS PATIENTS TAKING NSAIDS

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Objectives: To determine the efficiency of HELIC Ammonia Breath Test or HELIC ABT (AMA, Russia) for diagnostics of *H. pylori* (Hp) in stomach in rheumatoid arthritis patients taking NSAIDs. Materials and methods. Blind, diagnostic, cross-section study of 47 patients (the mean age 54.2 ± 12.5 years, 7 men and 40 women) with application of Latin square (table 2 × 2) for HELIC ABT was carried out. Examination of *H. pylori* infection in gastric mucosa by Giemsa was used as comparison method. Examination of *H. pylori* from 5 parts of the gastric mucosa (2 biopsy specimens from the body, one biopsy sample from the corner, two biopsies from the antrum part of the stomach) was carried out. All patients were treated with 7.5–15 mg of methotrexate per week, and 200–400 mg of nimesulide or 7.5–15 mg of meloxicam per day. Duration of 1 year. Results of estimation of efficiency HELIC ABT %(95% CI): sensitivity (Se) – 94 (83–100); specificity (Sp) – 90 (79–100); prevalence (P) – 38 (30–46); test accuracy (TA) – 92 (84–100); negative predictive value (−PV) – 96 (86–100); positive predictive value (+PV) – 85 (69–100); positive likelihood ratio (LR+) – 9.4 (3.0–27.1); negative likelihood ratio (LR−) – 0.07 (0.01–0.49). Conclusion: HELIC Ammonia Breath Test has high clinical efficiency (Se – 94%; Sp – 90%; TA – 92%) for diagnostics *H. pylori* in stomach in rheumatoid arthritis patients receiving long-term methotrexate and nimesulide or meloxicam.

Abstract no.: P10.11

HELICOBACTER PYLORI ANTIGEN-SPECIFIC ANTIBODIES ARE ASSOCIATED WITH GASTRIC HISTOPATHOLOGIC CHANGES

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Background: Serum screening of antigen-specific antibodies can ideally be used as a non-invasive and cost-effective method of monitoring *H. pylori*-mediated histopathologic changes. For this purpose, we have, herein, evaluated this hypothesis using three *H. pylori* recombinant proteins in association with *H. pylori* infection and its clinical outcomes.

Methods: Recombinant forms of cagA (3′- and 5′-fragments), napA and tip-alpha were expressed in E.coli pET expression systems and their identities were assessed by gene sequencing. Serum reactivity of Hp-infected (gastric cancer and NUD patients) and non-infected subjects was assessed against the recombinant proteins by western blotting.

Results: Serum antibodies against the CagA N-terminal fragment was able to detect Hp infection ($p < 0.05$), but failed to segregate between GC and NUD Hp-infected subjects (OR = 1.057, CI = 0.56–1.99, $p = 0.863$). On the other hand, the CagA C-terminal-specific antibodies were associated with the intensity of gastritis (OR = 3.78, CI = 1.39–10.31, $p = 0.009$) and atrophy (OR = 1.97, CI = 1.80–3.53, $p = 0.023$). Possession of serum antibodies against the recombinant Hp-NapA protein, increased the risk of gastric cancer by 2.6 fold (CI = 1.039–6.872, $p = 0.042$) in comparison with NUD subjects. Accordingly, serum antibodies against the recombinant Tip Alpha protein were associated with an estimated 10 fold enhanced risk of gastric cancer (OR = 9.71, CI = 1.51–63.32, $p = 0.017$), which was further prominent in cardia type GC (OR = 12.97, CI = 1.33–126.46, $p = 0.027$).

Conclusion: Serum profiling of *H. pylori* antigen-specific antibodies in combination with other intensifying risk factors, can identify subjects at higher rates of *H. pylori*-mediated gastric histopathologic changes. Well-designed validation studies are, however, required to recommend these assays for clinical applications.

Abstract no.: P10.12

A SIMULTANEOUS DUAL ANTRAL AND CORPUS RAPID UREASE TEST INCREASES THE DIAGNOSTIC YIELD FOR HELICOBACTER PYLORI INFECTION

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Introduction: Rapid Urease Tests (RUTs) provide simple and convenient methods of detecting H.pylori infection. False negative results can occur with gastrointestinal bleeding, atrophy and PPIs. In addition H.pylori infection rates are falling and could also affect the accuracy of a standard antral RUT.

Aims: To compare the clinical performance of single versus dual RUT's.

Method: Patients undergoing a routine gastroscopy aged 18–80 years were recruited. Demographics and PPI use were recorded. Single antral and a combined antral and corpus RUT tests were performed. Additional antrum and corpus biopsies were histologically assessed using Giemsa staining. *H. pylori* infection was defined by any positive test. The positivity rates and accuracy of single and dual RUT's were calculated and compared to histological data.

Results: 123 patients, 64 (52%) men, aged 51 ± 14.2 years (range 0–80), 44 (36%) on PPI, were recruited. *H. pylori* infection was diagnosed in 36% (n = 44), 30% (n = 37) by RUT and a further 7(16%) on histology. There was a significant difference in positivity between single and dual RUTs, 20% (n = 25) versus 30% (n = 37), $p < 0.0004$, (95% CI-0.15—0.04). All positive single RUT's were positive on dual RUT. Dual RUT's improved sensitivity and NPV compared to single RUT, 84% v 57% and 92% v 80% respectively. PPI use was associated with a great risk of false negative RUT's, 47% (9/19) v 8% (2/25); OR 6 (95%CI1.4–24.2).

Conclusions: A simultaneous dual antral and corpus RUT significantly increases diagnostic yield and negative predictive value without increasing cost and may become the standard practice.

Abstract no.: P10.13

PEPSINOGEN II (PGII) AND HP IGG IN HP-RELATED GASTRITIS DIAGNOSIS – A PROSPECTIVE CONTROLLED STUDY

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Background: PGII is an inflammation marker, IgG antibodies against Hp identify the bacterium presence in the stomach. The simultaneous analysis of these two markers is able to identify gastric mucosa damage mediated by Hp infection.

Material and Methods: We consecutively enrolled 144 patients with endoscopical diagnosis of non atrophic gastritis Hp-related and 127 patients with dyspepsia Hp negative. Every patient had upper GI endoscopy with biopsies and Gastropanel. Endoscopists, pathologists and laboratorists performed exam blindly each others.

Results: 1) PGII in non atrophic gastritis patients was 18.67 ± 10.55 and it was 7.07 ± 3.67 in patients with dyspepsia Hp negative ($p = 0.000$). IgG antibodies against Hp in non atrophic gastritis patients were 54.65 ± 21.08 and 15.64 ± 10.08 in patients with dyspepsia Hp negative ($p = 0.000$). 2) By means of ROC curve analysis we identifyed the best value for sensitivity and specificity of Hp infection. It was 9.5 μg/L for PGII and 26.5 EIU for IgG antibodies against Hp.

Conclusions: PGII and IgG antibodies against Hp are able to discern gastritis Hp-related versus gastritis Hp negative.

Abstract no.: P10.14

AMA RAPID UREASE TEST (AMA RUT) FOR DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION IN CHILDREN

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Introduction: AMA RUT is widely applied for diagnosis of *Helicobacter pylori* infection in Russia. This is a biochemical method that determines a high urease activity of *H. pylori* bacteria in the stomach biopsies. Determination of urease activity in biopsy is based on the color change of the indicator in the medium alkalization with ammonia, formed by hydrolysis of urea. AMA RUT doesn't demand incubation, is carried out at the room temperature and the same biopsy specimen can be examined directly after the 3-minutes period for further analysis, such as culture, histology etc.
Study aim: To study the efficiency of AMA RUT for diagnosis of *Helicobacter pylori* infection in children which were observed in a Children's city clinical hospital № 5 in period of 2012–2014 years.
Material and methods: On the basis of Children's city clinical hospital № 5 we studied 1824 children from 7 to 17 years old with gastroduodenal diseases. All children underwent diagnostic fibrogastroduodenoscopy with taking biopsy from the antrum of the stomach and followed AMA RUT with taken biopsy specimen. As a referent method for confirmation of HP status of the patient histology was used.
Results: According to histology data the bacteria *Helicobacter pylori* was found in 1116 patients (61%). The sensitivity and the specificity of AMA RUT was 89.3% and 92.9% respectively.
Conclusions: AMA RUT is cheap, fast, convenient and high sensitive and specific method for diagnosis of *Helicobacter pylori* infection in children.

Abstract no.: P10.15

UREA BREATH TEST AND SEROLOGICAL TEST HAVE EQUIVALENT ACCURACY TO DETECT *HELICOBACTER PYLORI* IN PATIENTS WITH GASTRODUODENAL ULCER BLEEDING

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Backgrounds: In case of bleeding, previous medications or low bacterial load, accuracy to *Helicobacter pylori (H.pylori)* tests can be decreased. This study aimed to compare a diagnostic accuracy of the four *H.pylori* tests (rapid urease test (RUT), C^{13}-urea breath test (UBT), serology and histology) in gastroduodenal ulcer bleeding.
Methods: From March 2008 to February 2013, we enrolled a total of 204 patients with gastroduodenal ulcer bleeding consecutively. All patients were performed the esophagogastroduodenoscopy within 48 hours at admission, and got at least two tests to detect *H. pylori* infection. Logistic regression with generalized estimating equation method was used to compare sensitivity or accuracy among tests.
Results: The mean age of the patients was 64.1 ± 15.4. Comparison of sensitivity and accuracy to detect *H. pylori* in patients with ulcer bleeding summarized in table.

Test	Sensitivity (%)	95%CI		Accuracy (%)	95%CI	
Histology	63.3	54.254	72.351	74.4	67.5068	81.2111
RUT	72.2	65.13	80.325	80.9	75.2265	86.4757
Serology	86.1	78.123	94.099	89.6	83.4725	95.6941
UBT	84.8	76.895	92.725	87.9	81.4496	94.3079

There was no difference of sensitivity or accuracy between UBT and serology ($p = 0.86$). Sensitivity or accuracy of RUT and histology decreased significantly to compare with UBT or serology. When RUT was gotten in two different sites, its accuracy was not inferior to UBT or serology.
Conclusion: This study recommend to test UBT or serology for determining the presence of *H. pylori* infection in patients with gastroduodenal ulcer bleeding in even high *H. pylori* prevalence area. If RUT is performed, it should be tested in two different sites.

Abstract no.: P10.16

IS THE BASAL VALUE OF UREA BREATH TEST A PREDICTIVE FACTOR FOR ANTIBIOTIC RESISTANCE AND SUCCESSFUL *HELICOBACTER PYLORI* ERADICATION?

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Background: Urea breath test (UBT) is a non-invasive method for *Helicobacter pylori* (Hp) diagnosis. Its' basal value, expressed as delta over baseline (DOB), could have a correlation with bacterial density and eradication rate.
Objective: Evaluate if UBT pretreatment values can predict Hp eradication and resistance to antibiotics.
Patients and Methods: One hundred and ninety-seven patients (females-66.5%; mean age-43.9 ± 14.5 years; residence in urban area-44.7%; chronic alcohol consumption-27.9%; smokers-11.2%), who received first-line eradication treatment with amoxicillin, clarithromycin and pantoprazole for 14 days, were included. For one hundred of them Hp resistance patterns to clarithromycin, levofloxacin and metronidazole were available.
Results: Successful eradication was achieved in 72.6% of cases. Therapeutic compliance was high (95.9%) and did not interfere with treatment success. Males had higher Hp eradication rates (81.8% vs 67.9%; OR = 2.13; CI 95% 1.03–4.35). The other epidemiologic variables didn't affect eradication. The following resistance patterns were detected: clarithromycin-22%, levofloxacin-27% and metronidazole-30%. Pretreatment DOB values were similar for patients with or without eradication success (41.2 ± 22.2 vs 44.1 ± 25; $p = 0.673$), resistance or susceptibility to clarithromycin (44.8 ± 27.6 vs 39.8 ± 22.8; $p = 0.567$) and metronidazole (36.7 ± 23.2 vs 42.8 ± 24.1; $p = 0.266$). However, DOB values were significantly higher in patients with levofloxacin-resistant Hp (48.8 ± 25.6 vs 38 ± 22.7; $p = 0.043$).
Conclusions: Pretreatment DOB values do not predict Hp eradication success with first-line empiric triple therapy as well as clarithromycin or metronidazole Hp resistance. However, higher initial values were observed in patients with levofloxacin resistant Hp, and that can help us to choose first-line therapy, by avoiding empiric use of this antibiotic.

Abstract no.: P10.17

VIDEO CAPSULE ENDOSCOPIC DIAGNOSIS OF HP INFECTION

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Background: In Japan, since February 2013, Eradication for HP infection has been covered by the National Medical Insurance. Accordingly, the National Medical Insurance emphasizes on endoscopic observation before the eradication.
Aim: To clarify possibility of HP infection by using Video capsule endoscopy (VCE).
Method: VCE we employed was PillCam SB2, Given Imaging, Yoqneam, Israel. We have been carrying out VCE for small intestine on 711 cases until now. Of the 711 cases, there were 69 cases who had received stool antigen test (SAT)and blood antibody test(BAT). We selected the presence of xanthoma, exudate, metaplasia as endoscopic findings of HP positive and fundic gland polyp (FGP), linear erythema (LE) as HP negative. We examined each sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).
Results: As a result of SAT and BAT, the number of HP positive cases was 49 and that of HP negative cases was 20. Median gastric observation time was 129.6 minutes. The sensitivity (%) of xanthoma, exudate, ulcer, metaplasia, FGP, LE by VCE were 71.4, 69.4, 73.4, 70.0 and 65.5. The specificity were 95.4, 70.0, 90.0, 98.0 and 91.8 respectively. The PPV were 97.2, 85.0, 94.7, 93.3 and 76.5 respectively. The NPV were 57.6, 51.7, 58.1, 58.9 and 86.5 respectively.
The successively eradication rate was 95.9% (47/49).
Conclusion: We are able to diagnose presence of HP by using VCE.

Abstract no.: P10.18

COMPARISON BETWEEN THE VISUAL AND AUTOMATIC INTERPRETATION OF HELIC ABT WITH INDICATOR TUBES

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HELIC Ammonia Breath Test (HELIC ABT) indicator tubes are sensitive single-use sensors that change color from initial (yellow or pink) to target color of dark blue. The length of the column with the target color is proportional to contents of ammonia in the air of the patient's mouth cavity. Apart from the target color green and grey colorations may occur, causing difficulties in the results interpretation, especially in different light conditions and due to peculiarities of human eye perception.

Aim: To compare visual and automatic reading and interpretation of the HELIC ABT indicator tubes colorations and results.

Method: Measuring ammonia presence in mouth cavity before and after a portion of unlabelled 12C urea was taken by means of conventional HELIC ABT with indicator tubes with visual interpretation of the result and by HELIC ABT Reader with automatic interpretation (CMOS sensor and a specialized software prototype). 25 patients were tested (15 adults, 10 children).

Results: There was a 96% concordance between the results of the visual and automatic interpretation, The automatic system could provide a better accuracy (resolution up to 0.2 mm) compared to a human eye and could precisely distinct color gradations that are natural for indicator tubes.

Conclusion: Automatic reading of the HELIC ABT indicator tubes is an approach that provides better accuracy and opens a scope of tasks to specify various aspects of HELIC ABT method in further research work.

Abstract no.: P10.19

COMPARISON OF BIOHIT *HELICOBACTER PYLORI* UFT300 QUICK TEST (LIQUID TEST) AND *HELICOBACTER PYLORI* QUICK TEST (GEL TEST) IN DETECTION OF *HELICOBACTER PYLORI* INFECTION IN A CLINICAL SETTING IN ST. PETERSBURG

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Background: To complement its *Helicobacter pylori* quick test (HPQT), Biohit Oyj (Helsinki, Finland) recently launched an ultra-fast BIOHIT *Helicobacter pylori* UFT300 quick test (UFT300). Both tests are intended for rapid diagnosis of *H. pylori* based on the detection of bacterial urease activity in the gastric biopsy.

Objective: To clinically validate the HPQT and UFT300 test among gastroscopy referral patients in a high-prevalence setting for *H. pylori* in St. Petersburg (Russia), using biopsy-confirmed *H. pylori* detection, PCR and cultivation as gold standards.

Methods: Patients (both genders, >45 years of age) for the cohort are enrolled among the patients attending the outpatient Department of Endoscopy at Clinical Hospital #122 (Sokolov) (St. Petersburg, Russia). All patients are subjected to gastroscopic examination, with directed biopsies from the antrum and corpus for the HPQT and UFT300. Final statistical analyses include calculation of the performance indicators for the two tests using three gold standards: (i) biopsy-confirmed *H. pylori* (ii) *H. pylori* cultivation, and (iii) *H. pylori* PCR genotyping.

Results: During May 2014, 50 subjects have been examined by the two tests. Altogether, 11(22%) and 13 (26%) subjects tested positive with HPQT and UFT300 tests, respectively. Agreement between the two tests is almost perfect; using Cohen's kappa $\kappa = 0.891$ (95% CI 0.740–1.000), and weighted kappa (ICC); $\kappa = 0.944$ (95% CI 0.902–0.968) (two-way random-effects model). The concordance between HPQT and UFT300 is 48/50 (96.0%). Biopsy data are pending at this writing.

Conclusion: HPQT and UFT300 seem to perform concordantly, capable of detecting *H. pylori* infection in gastric biopsies accurately within 30 and 5 minutes, respectively.

Abstract no.: P10.20

ENDOSCOPIC DIAGNOSIS OF *H. PYLORI* INFECTION USING LASEREO WITH A NOVEL IMAGE ENHANCEMENT

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Background: One of the most important endoscopic findings that suggested *H. pylori* infected mucosa is diffuse redness on fundic gland area. However, diagnosis of diffuse redness is sometimes difficult because of a lack of objectivity. The aim of this preliminary study was to evaluate the possibility of *H. pylori* diagnosis using LASEREO with a novel image enhancement.

Methods: The subjects who received endoscopic examination using LASEREO system (FUJIFILM, Tokyo, Japan) and diagnostic test of *H. pylori* were enrolled. Diagnosis of *H. pylori* infection depends on more than two accordant results among diagnostic tools. This novel image enhancement by combination of BLI-bright pre-processing image and post-processing emphasizes the mucosal color, especially the difference between the slight redness and normal mucosa. The diagnosis of *H. pylori* was compared with the color of a novel image on fundic gland area.

Results: In 29 subjects without eradication therapy, the color of a novel image were bright redness in 94% of patients with *H. pylori* positive and dark gray in all of patients with *H. pylori* negative. In 15 subjects after successful eradication therapy, 3 were misdiagnosed as *H. pylori* positive. One subject after failed eradication was correctly diagnosed.

Conclusion: Diagnosis of diffuse redness was made easier using a novel image enhancement. It is useful to endoscopic diagnosis of *H. pylori* infection.

Abstract no.: P10.21

LATEX AGGLUTINATION TEST FOR DETECTION OF *H. PYLORI* IN GASTRIC BIOPSIES

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Introduction: No test for detection of *H. pylori* (HP) in gastric mucosa (culture, microscopic examination, histology and PCR) is 100% sensible and specific. We propose a novel technique to reveal the presence of HP in the stomach of dyspeptic patients, the latex agglutination test (LAT).

Patients and Methods: Forty-one dyspeptic patients underwent upper endoscopy; biopsies were taken from the antrum and fundus for culture, histology and bacterioscopy. Latex particles were sensitized with sera obtained in rabbit against whole HP antigens and CagA. Biopsies were dissolved in PBS with 0.1% dithiothreitol on a slide; one drop of sensitized latex suspension was added and, in the presence of HP antigens, agglutination was observed within 1 minute. In HP positive cases by gold standard (GS, concordant results of culture and histology), we determined the CagA serological status by ELISA.

Results: HP was detected in 21 patients (51.2%). LAT was positive in 20 cases (sensibility = 95.2%) and negative in 18 of the 20 negative cases (specificity = 90%). Standard serology showed serum antibodies in the two "false positive" cases; coccoid organisms were also seen in one of these samples. Serology revealed anti-CagA serum antibodies in 12 cases out of the 21 infected patients (57.1%). LAT was positive in 10 cases (sensibility = 83.3%) and negative in 8 out of the 9 negative by ELISA (specificity = 88.8%).

Discussion: This novel test has good sensibility and specificity. LAT may also detect coccoid *H. pylori* organisms, thus performing better than GS in some cases.

Abstract no.: P10.22

THE DIAGNOSTIC ACCURACY OF *HELICOBACTER PYLORI* ANTIGEN DETECTION IN DUODENAL JUICE

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Helicobacter pylori (Hp) stool antigen tests are widely used to diagnose current Hp infection as an alternative to the invasive techniques. Data regarding the detection of Hp antigens in other sources, such as gastric or duodenal juice, are limited.

Aim: To study the diagnostic accuracy of Hp antigen detection in duodenal juice with comparison to Hp stool antigen test.

Methods: 46 adolescents aged 11–17 years with recurrent abdominal pain referred to a pediatric gastroenterology center (Krasnoyarsk, Russia) were tested to Hp presence in stool and duodenal juice. Duodenal secretions are collected by continuous aspiration via nasogastric tube. Stool and duodenal juice samples were frozen at −20°C. Hp antigen ELISA monoclonal test (Immundiagnostik, Germany) was used. Data are shown with 95% confidence interval.
Results: Hp antigen was detected in 28% (23/46) stool samples and in 6% (5/46) duodenal juice samples. Sensitivity Hp antigen detection in duodenal juice with comparison to Hp stool antigen test was 22 (9–42) %, specificity – 100 (82–100) %, positive predictive value – 100%, negative predictive value – 55 (40–70) %.
Conclusion: Hp antigen detection in duodenal juice has high sensitivity but extreme low sensitivity that may be explained by high level of antigens dilution by liquid components.

Abstract no.: P10.23

CURRENT STATUS OF *H. PYLORI* ISOLATES RESISTANCE TO RIFABUTIN AND RIFAMPIN IN IN IRAN

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Introduction: *Helicobacter pylori* infection persists in a considerable proportion of patients after both first-and second-line current treatments and the ideal regimen to treat this infection has still to be found. Preliminary in vitro studies have shown that *H. pylori* is highly susceptible to rifabutin. In this study resistance to rifabutin and its structurally related antibiotic, rifampin was assessed.
Methods: One hundred *H. pylori* isolates from dyspeptic patients were recruited in this study. Bacterial suspensions (MacFarland No. 2) were surface inoculated on Brucella blood agar. Sterile blank disks were deposited on the surface of inoculated plates and 10 µL volume of rifabutin (0.06 µg/mL) and rifampin (4 µg/mL) was introduced into the blank disk. After 3–5 days of microaerobic incubation the inhibition zone diameters (IZDs) were recorded.
Results: Among 100 isolates, 6 isolates exhibited IZDs <20 mm and considered resistant to rifabutin. Resistance to rifampin was found in 13 isolates. Rifabutin and rifampin were considerably effective on the susceptible strains which produced IZDs of 20–60 mm and 20–45 mm, respectively. Only one isolate was resistant to both antibiotics. There was no significant difference between resistance rates to rifabutin and rifampin (p value > 0.05).
Discussion: Eradication of *H. pylori* infection is a primary goal in the management of *H. pylori*-related complications According to our finding, resistance of *H. pylori* isolates to rifabutin and rifampin is low, 6% and 13%, respectively. High efficacy of rifabutin and rifampin could make them good choices in quadruple and rescue therapy regimens for eradication of *H. pylori* in Iran.

Abstract no.: P10.24

THE INFLUENCE OF PPI CONSUMPTION ON THE RESULT OF RAPID UREASE TEST (RUT) AND CULTURE OF *HELICOBACTER PYLORI* (HP)

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Aim: To compare the results of RUT and culture of gastric biopsies for diagnosis of *HP* infection in dyspeptic patients who consumed PPI.

Methods: Two antral biopsies from 539 dyspeptic patients were taken, one for RUT and one for culture.
Results: Among 539 biopsies, 213 (39.51%) were urease positive and 326 (60.48%) were urease negative. Among urease positive biopsies, 186 (89.32%) were culture positive and 27 were culture negative. Among 326 urease negative biopsies 31 (9.50%) were culture positive and 295 (90.49%) were culture negative. Table 1 shows the relationship between RUT, culture and PPI consumption.

539 biopsies				
RUT	213 RUT positive (39.51%)		326 RUT negative (60.48%)	
Culture	186 culture positive	27 culture negative	31 culture positive	295 culture negative
No PPI consumption	110 (59.13%)	13 (48.14%)	9 (29.03%)	66 (%25.76)
PPI consumption	76 (40.86%)	14 (51.85%)	22 (70.96%)	219 (%74.23)

Discussion: Most of biopsies that were RUT and culture positive belonged to patients without consumption of PPI. However, among RUT negative and culture positive biopsies there were considerable numbers that were related to patients who consumed PPI. It is concluded that PPI consumption leads to false negative RUT result. This could mislead the diagnosis of HP infection.

Abstract no.: P10.25

THE EFFECT OF PPI CONSUMPTION ON THE DIAGNOSIS OF *H. PYLORI* INFECTION BY RAPID UREASE TEST (RUT), CULTURE AND STAINED BIOPSY SMEARS

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Aim of this study was to compare the results of RUT, culture and biopsy smears in patients who consumed PPI with those that did not. Two gastric biopsies were taken from 153 dyspeptic patients and their history of PPI consumption was recorded. First biopsy was used for RUT and the results were recorded as positive when turned pink within 2 hours and delayed positive if turned pink within 24 hours. Second biopsy was used for culture and preparation of direct smears. Smears were Gram- stained and examined for the presence of *H. pylori* by light microscope. Results are shown in table below.Among 153 patients, 67 (43.8%) consumed PPI and 86 (56.2%) did not. The number of patients with positive results of RUT, culture and biopsy smears and without PPI consumption (49, 59%) was more than twice of those who consumed PPI (23, 27.7%). Of total 67 patients with PPI consumption, 11 (16.4%) biopsies were RUT negative and culture positive with 8/11 (27.7%) showing smear negative results. Delayed urease activity was only detected in patients with PPI consumption (8/153, 5.2%) compared with those without (0, 0%). It is concluded that frequent consumption of PPI in Iran could lead to false negative results of RUT and biopsy smears probably due to inhibitory effect on urease activity and reduced number of bacteria in biopsy smears.

153 biopsies RUT results in 83 smear (+) samples							RUT results in 70 smear (−) samples					
RUT +			Delayed RUT +		RUT−		RUT +		Delayed RUT +		RUT −	
Patients	Culture +	Culture −	Culture +	Culture −	Culture +	Culture −	Culture +	Culture −	Culture +	Culture −	Culture +	culture −
PPI consumption 67 (43.8%)	23 (27.7%)	2	3	0	3	1	20 (28.6%)	1	3	2	8 (11.4%)	1
No PPI consumption 86 (56.2%)	49 (59%)	1	0	0	0	1	32 (45.7%)	0	0	0	2 (2.9%)	1

Abstract no.: P10.26

HELICOBACTER PYLORI ERADICATION IN DUODENAL ULCER: WHAT ERADICATION RATES? WHAT IMPACT ON ENDOSCOPIC HEALING?

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Aims: To compare *Helicobacter pylori* eradication rates between dyspepsia and Duodenal ulcer (DU) and to appreciate the concordance between Hp post treatement eradication and DU healing.

Methods: From 2002 to 2011, 392 Hp positive patients have been enrolled in this prospective and unicentric study (mean age: 37.3 years, men: 126, dyspepsia: 300, DU: 92). DU was diagnosed at upper endoscopy and was defined as open ulcer of ≥5 mm. Patients have been treated during 7–10 days with OAM10 triple therapy or OAC7 regimen.The Controls of the healing ulcer and Hp eradication were performed 12 weeks after treatment. The success of anti *H. pylori* treatment was attested by the negativity of 4 tests: 13C-Urea Breath Test, Rapid Test Urease + histology and culture.

Results: In ITT, respective eradication rates in DU and dyspepsia were 69, 5% and 61.5% (P:0.19). PP rates were 76.1% and 61.9% (p:0.21). Endoscopic DU control was performed in 74 patients. 82.4% (47/57) among them have completely healed after Hp eradication. In the oher hand, 20% (07/17) of DU have totally healed despite the failure of anti Hp treatment. Statistical analysis showed a significant difference in favor of the positive effect treatment success ($p < 0.05$). Thus, the concordance between Hp eradication and healing of DU was intermediate (kappa coefficient: 0.4).

Conclusion: Our study showed a positive effect of Hp eradication on DU healing. Nevertheless, their concordance was not good. These results are in favor of the continuation of PPI after the end of DU anti Hp treatment.

Abstract no.: P10.27

WHAT KIND OF ENDOSCOPIC FINDINGS RELATE TO *H. PYLORI* INFECTION?

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Background: In this study, we investigated the relationship between *H. pylori* infection and endoscopic findings and diagnoses chronologically.

Subjects and Methods: The subjects were 418 patients who underwent *H. pylori* serological test and endoscopy. Endoscopic diagnoses available were red streaking (RS), regular arrangement of the collecting venules (RAC), fundic polyps (FP), hyperplastic polyps (HP), endoscopic raised erosive gastritis (EREG), endoscopic flat erosive gastritis (EFEG), endoscopic atrophic gastritis (EAG: more than moderate), endoscopic erythematous/exudative gastritis (EE/EG), endscopic congestive gastropathy (ECG), endoscopic haemorrhageic gastritis (EHG), endoscopic rugal hyperplastic gastritis (ERHG), gastric xanthoma (GX), and nodular gastritis (NG).

Results: Infection rates by age group were: 20 seconds 15.7% (11/70), 30 seconds 28.0% (42/150), 40 seconds 34.3% (49/143), and 50 seconds 69.1% (38/55). For people in their 20 seconds RAC was only related with *H. pylori* (−), EAG was only significantly related with *H. pylori* (+). RS, FP and RAC were significantly related with *H. pylori* (−) for people in their 30, 40, 50 seconds. On the other hand, EE/EG, ECG, ERHG and AG were also significantly related with *H. pylori* infection-positive for people in their 30, 40, 50 seconds. Moreover logistic regression analysis revealed RS: 0.15 (0.042–0.542), RAC: 0.045 (0.016–0.124) and EAG: 11.87 (4.06–34.7) were significantly related with *H. pylori* infection.

Conclusions: Hereafter, we should take age into consideration with reference to the endoscopic findings of *H. pylori* infection.

Abstract no.: P10.28

INVASIVE METHOD FOR EXPRESS DETECTION OF GASTRAL UREALYTIC MICROFLORA DURING THE STOMACH ENDOSCOPY

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Introduction: Problems of biopsy material representativeness and delays in antimicrobial treatment's initiation, related to the procedure of the histology, necessitate the search of new highly sensitive diagnostic methods. The proposed diagnostic method of urealytic microflora semination in stomach doesn't require biopsy and its laboratory testing. Diagnostic conclusion is formed just after performing stomach endoscopy. The method is based on ammonia production in urea hydrolysis in the presence of gastric urease.

Materials and Methods: The experiment included 12 patients of the gastroenterological department, 9 patients suffered from histologically confirmed infection *Helicobacter pylori*. Stomach walls of each patient were flushed with 50 mL 1% urea solution during the gastroscopy. Before gastroscopy and right after it the ammonia level in the oral cavity of patients was measured within 9 minutes with each second registration of concentration values.

Results: Reliable change ($p < 0.001$) of empiric distribution of the ammonia concentration in the oral cavity was found in 11 patients, which certifies the start of urea hydrolysis in the presence of gastric urease.

Discussion: Direct exposure on urealytic microflora by urea solution in combination with NH_3 concentration control in oral cavity allows obtaining diagnostic results free from target biopsy errors.

Conclusions: The proposed invasive express-method outdoes the histological methods taken as a golden standard in terms of sensitivity, and also possesses lower cost and time for obtaining diagnostic results, with total time of the endoscopic investigation decreased.

Abstract no.: P10.29

DETERMINING SENSITIVITY AND SPECIFICITY OF MON-HP RAPID UREASE TEST

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Background: *H. pylori* infection is high in Mongolia but diagnostic tests including histology; rapid urease test and bacteriology were far from routine practice in our country. Here we are evaluating newly produced MON-HP rapid urease test, developed by Innovation project, Science and Technology Foundation.

Aim: Determining sensitivity, specificity of MON-HP rapid urease test.

Materials and Methods: Totally 67 consecutive patient underwent upper gastrointestinal endoscopy with 3 antral biopsies for CLOtest, histology and MON-HP test. MON-HP urease test results were interpreted after 3 hours.

Results: Of the 67 patients undergoing rapid urease testing, 37% were male and 63% were female, with a mean age of 35 years (range 18–62 years). Histological examination revealed *H. pylori* in 64.2% (N = 43) of the biopsy specimens. Out of 67 cases, 42 (62.6%) were positive for CLOtest and 43 (64.2%) were positive for MON-HP test. There were 2 false positive and 3 false negative tests in MON-HP comparing histopathology. One of these 2 false positive results could be accounted for by a low *H. pylori* density in histological examination. The sensitivity, specificity, PPV and NPP of MON-HP were 93%, 91.7%, 95% and 88%, respectively. Comparing to CLOtest, there was one false positive result in MON-HP test.

Conclusion: This study shows MON-HP has good accuracy comparing histopathology and commercially available CLOtest for detection of *H. pylori* infection (Kappa coefficient 0.8-0.9 $p < 0.001$).

Abstract no.: P10.30

INHIBITORY EFFECT OF OMEPRAZOLE AND LANSOPRAZOLE ON THE UREASE ACTIVITY OF *H. PYLORI*

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Aim: Urease plays an essential role in the persistence and colonization of *H. pylori* in the stomach. Detection of urease activity is an easy, rapid and powerful tool for detection of *H. pylori* infection in endoscopy rooms. In this study anti-urease activity of omeprazole and lansoprazole was examined.

Methods: Two *H. pylori* isolates were treated with different dilutions of omeprazole and lansoprazole (256, 192, 128, 64, 32 and 16 μg/mL) in saline for 0, 5, 10, 15, 20, 25 and 30 minutes. One hundred μL samples were taken from each dilution and added to 50 μL of rapid urease test solution (urea and phenol red). The time needed for color change to pink (compared to control; without PPIs) and the concentration of PPI that inhibited color change was recorded.

Results: Omeprazole and lansoprazole at the concentration of 256 μg/mL could inhibit the urease activity of *H. pylori* and the inhibition persisted for more than 3 hours. Color change to pink happened at concentrations lower than 256 μg/mL. Omeprazole showed stronger inhibitory effect than lansoprazole.
Discussion: Omeprazole and lansoprzole inhibited the urease activity of *H. pylori*. It can be proposed that consumption of omeprazole or lansoprazole by dyspeptic patients could lead to misinterpretation of rapid urease test in endoscopy rooms. Accordingly, patients need to be advised to stop taking PPIs before endoscopy in order to avoid false negative results of *H. pylori* urease activity.

Abstract no.: P10.31

IS SERUM ANTIBODY TEST SUFFICIENT TO MAKE THE PRECISE DIAGNOSIS OF *HELICOBACTER PYLORI* INFECTION IN UPPER GASTROINTESTINAL BLEEDING?

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Background: Gastroduodenal ulcer and gastric cancer are common cause of upper gastrointestinal bleeding (UGIB). There are mostly associated with *Helicobacter pylori* (Hp) infection. Although serum Hp antibody test is widely used in the diagnosis of Hp infection, the frequency of false negative for serum antibody test in UGIB remains obscure.
Method: From January 2013 to December 2013, 70 adults with UGIB were diagnosed as gastroduodenal ulcer or gastric cancer. They were checked with serum Hp antibody test initially. Subsequently, feces Hp antigen test was added in cases of negative for serum Hp antibody test. We analyzed the ratio of false negative for serum Hp antibody test.
Result: 62 cases were at least positive for either serum antibody or feces antigen. The positive results of serum antibody were obtained in 40 cases of the gastric ulcer (n = 54), 8 cases of the duodenal ulcer (n = 10), and 3 cases of the gastric cancer (n = 5). The feces antigen test revealed positive in 7 cases of the gastric ulcer with negative for serum antibody (n = 14), 2 cases of the duodenal ulcer with negative for serum antibody (n = 2), and 2 cases of the gastric cancer with negative for serum antibody (n = 3). As a whole, false negative for serum antibody were confirmed in 11/62 (17.7%). Among patients negative for serum antibody, feces antigen test revealed positive in 11/19 (57.8%).
Conclusion: False negative for serum Hp antibody test in UGIB were unexpectedly at the high rate.

Abstract no.: P10.32

CORRELATION OF IGG IMMUNE RESPONSES TO SELECTED *H. PYLORI* PROTEINS WITH DISEASE STATUS IN DIFFERENT POPULATIONS

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H. pylori colonizes half of the world's population, but only a minority of infected individuals develop associated diseases. Nevertheless, it is a major health problem because of its high worldwide prevalence and the link to ulcer, gastric cancer and MALT-lymphoma development. To date, it is not possible to non-invasively identify patients with progressed disease state. *H. pylori* virulence factors have been associated with disease development, but direct assessment of virulence factors up to now requires invasive methods to obtain gastric biopsies. Our study evaluated a new prototype of diagnostic test for serological detection of a *H. pylori* infection, using an improved selection of virulence factors. Moreover, we compared the performance of this prototype to the commercially available recomLine Helicobacter, using serum samples from different cohorts across the world (Germany, Italy, China, Mexico). In combination, the humoral responses against these antigens correlate with the severity of disease among *H. pylori*-positive subjects. In all populations the new antigen combination showed superior test results compared to the recomLine Helicobacter. In future this new combination of antigens could replace the commercially available recomLine Helicobacter.

P11 Clinical Trials and Novel Treatments

Abstract no.: P11.01

PAN-EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): FIRST-LINE TREATMENTS

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Introduction: Due to the diversity of regimens used as first-line treatment in the Hp-EuReg study, a separate abstract has been created to describe the efficacy of these treatments.

Aims and Methods: To evaluate the efficacy of first-line treatments prescribed in the Hp-EuReg.The methodology applied was that established on Hp-EuReg project.

Results: Up to now, 4518 *naïve* patients have been included. The most commonly used treatments in order of prescription were: PPI+clarithromycin+amoxicillin (32%); PPI+amoxicillin+nitroimidazole (26%); PPI+clarithromycin+nitroimidazole (17%); non-bismuth quadruple [concomitant (12%) and sequential (11%)]; bismuth quadruple (2%); others (1%).

Table 1 summarizes the results. Overall, in 6.3% of treatments eradication was not confirmed. 32% of first-line treatment failures were not retreated.

	Compliance	ITT (95% CI)	mITT (95% CI)
PPI+C+A			
7 days	97%	73% (69–77%)	76% (72–80%)
10 days	98%	76% (72–80%)	83% (80–87%)
	>Esomeprazole	82% (73–91%)	87% (79–95%)
14 days	99%	84% (79–89%)	89% (85–94%)
	>Esomeprazole	89% (82–96%)	90% (83–97%)
PPI+A+N			
7 days	98%	76% (71–80%)	81% (77–85%)
10 days	97%	75% (71–79%)	82% (79–86%)
	>Esomeprazole	83% (73–94%)	89% (80–98%)
14 days	99%	82% (75–89%)	85% (79–92%)
	>Esomeprazole	85% (74–96%)	85% (74–96%)
PPI+C+N			
7 days	98%	75% (70–80%)	83% (79–87%)
10 days	99%	79% (73–85%)	84% (79–89%)
	>Esomeprazole	84% (72–96%)	86% (75–97%)
14 days	99%	79% (71–88%)	89% (83–95%)
	>Esomeprazole	89% (79–99%)	92% (83–100%)
Bismuth quadruple			
10 days	100%	91% (83–98%)	92% (85–100%)
Concomitant			
10 days	93%	84% (78–90%)	87% (81–92%)
14 days	99%		
	>Esomeprazole	90% (87–94%)	92% (88–95%)
Sequential			
10 days	96.8%	87% (84–90%)	89% (86–92%)
	>Esomeprazole	90% (86–94%)	92% (88–96%)

ITT, intention-to-treat; C.I., confidence interval; PPI, proton pump inhibitor; C, clarithromycin; A, amoxicillin; N, nitroimidazols; mITT, modified ITT excluding those patients in which confirmation of eradication was not performed.

Conclusion: Most *H. pylori* eradication treatments prescribed by gastroenterologists in Europe are suboptimal, especially due to the frequent use of the standard triple therapy. Over 90% eradication rate was only achieved with: (i) bismuth-containing quadruple treatment; (ii) extending regimens to 14 days and/or using combinations including esomeprazole.

Abstract no.: P11.02

META-ANALYSIS OF SEQUENTIAL VERSUS STANDARD TRIPLE THERAPY FOR *HELICOBACTER PYLORI* ERADICATION: FINAL RESULTS OF A COCHRANE SYSTEMATIC REVIEW

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Introduction: Sequential therapy (SEQ) has been suggested as a new first-line treatment option to replace the standard triple therapy (STT), where eradication rates have declined to unacceptable levels.

Aims and Methods: To conduct a meta-analysis of studies comparing SEQ versus STT for *H. pylori* eradication.

Selection of studies: randomized controlled trials comparing SEQ (10-days) and STT (≥7-days) for the eradication of *H. pylori*. Search strategy: bibliographical searches in electronic databases, and manual search of abstracts from Congresses, were conducted up to November 2013. Data synthesis: intention-to-treat eradication rate.

Results: We included 33 randomized controlled studies with 9750patients (4542 SEQ and 5208 STT). The overall analysis showed that SEQ was significantly more effective than STT (84% vs 74% by intention-to-treat analysis; OR = 2.07; 95% CI = 1.64–2.61; $p < 0.001$). Results were highly heterogeneous ($I^2 = 77\%$) and 11 studies were unable to demonstrate differences between therapies. Subgroup analyses suggested that patients with clarithromycin resistance and/or taking esomeprazole-rabeprazole could benefit more from the SEQ. However there were no differences when STT lasted 14-days. Although, overall, mean eradication rate with SEQ was over 80%, a tendency towards lower efficacy with this regimen was observed in more recent studies [weighted linear regression −2% per-year in SEQ versus −0.5% per-year in STT], and in studies performed outside Italy (OR 1.57 vs 4.09).

Conclusion: The meta-analysis demonstrated that SEQ is more effective than STT lasting less than 14-days. Nevertheless, the apparent advantage of sequential treatment seems to be decreasing over time; therefore further and continuous assessment is needed before a generalized change in all settings is recommended for first line *H. pylori* treatment.

Abstract no.: P11.03

This abstract has been withdrawn.

Abstract no.: P11.04

H. PYLORI ERADICATION RATE IS INFLUENCED BY BACILLUS COAGULANS, LACTOFERRIN AND FRUCTOOLIGOSACCHARIDES AND NOT BY THE DOSAGE OF PROTON PUMP INHIBITORS

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Background: Increasing the dosage of PPI has been proposed to increase *H. pylori* eradication rate. Similarly, adding some adjuvants to a standard triple therapy, such as Lactoferrin, pre and probiotics may improve the successful of the cure. Whether the best strategy would be increasing the dosage of PPI or adding all those adjuvants to a standard triple therapy is not known.

Methods: 300 age and sex-matched patients were randomized into 3 different schemes: (i) Lansoprazole 15 mg/bid, Amoxicillin 1 g/bid, Clarithromycin 500 mg/bid for 7 days (LAC15); (ii) Lansoprazole 30 mg/bid, Amoxicillin 1 g/bid, Clarithromycin 500 mg/bid for 7 days (LAC30); (iii) Lansoprazole 15 mg/bid, Amoxicillin 1 g/bid, Clarithromycin 500 mg/bid for 7 days enriched with a mix of Lactoferrin, Fructooligosaccharides and Bacillus Coagulans tid for 15 days (LAC-LFB). Eradication was confirmed by UBT. Compliance and adverse effects were also assessed.

Results: Eradication rates were: LAC15 72%, LAC30 67% and LAC-LFB 85%. Eradication rates were similar in LAC15 and LAC30 (p = ns), while were higher in LAC-LFB compared to both LAC15 and LAC30LAC ($p < 0.02$). Interestingly, the occurrence of side effects was significantly lower in the group of LAC-LFB.

Conclusions: Adding a mix of lactoferrin, fructooligosaccharides and Bacillus coagulans and not increasing the dosage of PPI significantly increases the eradication rate of a standard clarithromycin based triple therapy. The concomitant reduced occurrence of antibiotic-related side effects make LAC-LFB a good first line regimen.

Abstract no.: P11.05

EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): SPANISH DETAILED RESULTS (INTERIM ANALYSIS)

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Introduction: Spain has a strong regional variety of resistance and efficacy rates in *Helicobacter pylori* treatment. It seems necessary to provide updated data of daily clinical practice in order to design the best strategies to achieve better eradication results.

Aim: To systematically register Spanish gastroenterologist's clinical routine management of *H. pylori* infected adult patients.

Methods: Observational, prospective, multicenter study, carried out in 23 Spanish hospitals as part of the 'Pan-European Registry on *H. pylori* management. Clinical information is being registered by clinicians through an electronic clinical research file.

Results: 1720 patients have been included so far. 60% women Median age was 51 ± 15 years old. The most frequent diagnostic tests used were histology and 13C-urea breath test. Treatments most frequently prescribed as first line therapies were triple standard therapy with a PPI, amoxicillin and clarithromycin (48%), and non-bismuth quadruple (concomitant) therapy (42%). Efficacy rates obtained with standard triple therapy prescribed for 10 days with omeprazole (20 mg b.i.d.) and for 14 days with esomeprazole (40 mg b.i.d.) were 82% and 90%, respectively. When non-bismuth quadruple (concomitant) therapy was analyzed, if it was prescribed for 10 days and using omeprazole, the efficacy rate obtained was 84%; if duration was extended to 14 days and using esomeprazole, efficacy reached was 90%.

Conclusions: Data show a trend towards better results with regimens containing esomeprazole and lasting 14 days than for omeprazole and 10 days duration, independently of the antibiotic combination prescribed. Deeper analysis is required to provide clear recommendation regarding the best first-line treatment in Spain.

Abstract no.: P11.06

PAN-EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT (HP-EUREG): RESCUE TREATMENTS

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Introduction: Due to the diversity of regimens used as second-line treatment in the Hp-EuReg study, a separate abstract has been created to describe the efficacy of these treatments.

Aims and Methods: To evaluate the efficacy of second-line treatments prescribed in the Hp-EuReg. The methodology applied was that established on Hp-EuReg project.

Results: Up to now, 941 rescue treatments have been registered. The most commonly used treatments (61%) were quinolone-containing triple therapies (levofloxacin 69% and moxifloxacin 31%) and bismuth quadruple therapy (15%). The remaining treatments were too diverse and reduced in number to be evaluated. Overall, in 4.2% of treatments eradication was not confirmed, and 48% of rescue treatment failures were not retreated.

	Compliance	ITT (95% C.I.)
PPI+A+L		
10 days	99%	76% (70–82%)
	>Esomeprazole	89% (78–100%)
14 days	98%	93% (84–100%)
	>Esomeprazole	100% (82–100%)
PPI+A+M		
14 days	99%	
	>Esomeprazole	86% (79–93%)
Bismuth quadruple		
10 days	96%	59% (42–76%)
14 days	91%	66% (54–79%)

ITT, Intention-to-treat; C.I., confidence interval; PPI, proton pump inhibitor; A, amoxicillin; L, levofloxacin; M, moxifloxacin.

Conclusion: Quinolone-containing triple therapies offer acceptable results as rescue treatments in *H. pylori* eradication. Extending regimens to 14 days and/or using esomeprazole as the proton pump inhibitor may increase their efficacy.

Abstract no.: P11.07

HELICOBACTER PYLORI FIRST-LINE AND RESCUE TREATMENTS IN THE PRESENCE OF PENICILLIN ALLERGY

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Background: In patients allergic to penicillin, the most frequently recommended treatment contains a proton-pump-inhibitor (PPI), clarithromycin and

metronidazole. However, a bismuth-containing quadruple therapy may be preferred. Furthermore, *H. pylori* eradication is a challenge when a first treatment fails.

Aim: To assess the efficacy and safety of *H. pylori* first-line treatment with a PPI-clarithromycin-metronidazole triple therapy and a bismuth-containing quadruple therapy and of rescue regimens, in patients allergic to penicillin.

Methods: Design: Prospective multicenter study. Intervention: Patients allergic to penicillin were given a first-line treatment comprising: (i) 7-day omeprazole-clarithromycin-metronidazole; and (ii) 10-day omeprazole-bismuth-tetracycline-metronidazole. Rescue treatments: (i) Bismuth quadruple therapy(as previously defined); (ii) 10-day PPI-clarithromycin-levofloxacin; and (iii) 10-day PPI-clarithromycin-rifabutin. Outcome: Eradication was confirmed by 13C-urea-breath test 8 weeks after therapy. Compliance/tolerance: Compliance was determined through questioning and recovery of empty medication envelopes. Adverse effects were evaluated by means of a questionnaire.

Results: 267 consecutive treatments were included. (i) First-line treatment: Per-protocol and intention-to-treat eradication rates with omeprazole-clarithromycin-metronidazole were 59% (62/105; 95% CI = 49–62%) and 57% (64/112; 95% CI = 47–67%). Respective figures for PPI-bismuth-tetracycline-metronidazole were 75% (37/49; 95% CI = 62–89%) and 74% (37/50; 95% CI = (61–87%) ($p < 0.05$). Compliance with treatment was 94% and 98%, respectively. Adverse events were reported in 14% with both regimens (all mild). (ii) Second-line treatment: Intention-to-treat eradication rate with omeprazole-clarithromycin-levofloxacin was 64% both after triple and quadruple failure, compliance was 88–100%, with 23–29% adverse effects(all mild). (iii) Third/fourth-line treatment: Intention-to-treat eradication rate with PPI-clarithromycin-rifabutin was 22%.

Conclusion: In allergic to penicillin *H. pylori* infected patients, a first-line treatment with a bismuth-containing quadruple therapy (PPI-bismuth-tetracycline-metronidazole) seems to be a better option than the triple PPI-clarithromycin-metronidazole regimen. A levofloxacin-based regimen (together with a PPI and clarithromycin) represents a second-line rescue option in the presence of penicillin allergy.

Abstract no.: P11.08

THE IMPACTION OF *HELICOBACTER PYLORI* INFECTION, ANXIETY AND DEPRESSION IN PATIENTS WITH SUBGROUP OF FUNCTIONAL DYSPEPSIA IN THAILAND

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Background: Functional dyspepsia (FD) is one of the most common gastrointestinal diseases worldwide. *H. pylori* infection and psychosocial stressors frequently precede and exacerbate symptoms of FD. This study aimed to investigate prevalence and impaction of *H. pylori* infection, anxiety and depression in subgroup of FD in Thailand.

Methods: This cross-sectional study performed in tertiary care center of Thailand during February 2013-January 2014. FD patients were assigned to complete anxiety and depression questionnaires. *H. pylori* infection was detected by CLO-test, culture or histopathology. FD patients were diagnosed by Rome III criteria and categorized as epigastric pain syndrome (EPS) and postprandial distress syndrome (PDS). The anxiety and depression scores were analyzed by appropriate statistical analysis.

Results: 300 FD patients (174 female, 126 male with mean age of 54.8 ± 15.1 years) were enrolled. There were 108 EPS and 192 PDS patients. 23.3% of FD patients were infected with *H. pylori*. Anxiety and depression demonstrated in 23% and 7.3% of FD patients. *H. pylori* infection, anxiety and depression were significantly higher in PDS than EPS patients (27.1% vs 16.7%; p-value = 0.04; OR = 1.86, 95% CI = 1.01–3.53; p-value = 29.7% vs 11.1%; p-value = 0.0002; OR = 3.4, 95% CI = 1.7–7.1, 10.4% vs 1.9%; p-value = 0.006; OR = 6.2, 95% CI = 1.4–38.9 respectively).

Conclusions: *H. pylori* infection, anxiety and depression disorders were commonly found and might be important factors for developing FD especially PDS subgroup in Thailand. The management concern to these factors could be key success for treatment of Thai FD patients.

Abstract no.: P11.09

SEQUENTIAL VERSUS PROLONGED TRIPLE THERAPY META-ANALYSES MAY BE INFLUENCED BY "GEOGRAPHICAL WEIGHTING"

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Background: Sequential therapy is a first line regimen obtaining satisfactory *H. pylori* eradication. Triple therapy prolongation improves success rate even if recent meta-analyses showed fitting results only for 14-day regimen. Studies from Africa and North America were unavailable.

Aim: To perform a meta-analysis comparing sequential versus prolonged 10/14-day triple therapy with regard to "geographic weighting" by considering subgroups analysis according to metronidazole low and high resistance areas (HRa: Asia/South America/Africa vs LRa: Europe/North America).

Methods: Based on PRISMA recommendations, we considered all first-line clinical studies from 2003 to April 2014. Randomized clinical trials (RCTs) were included by a research in PubMed, MEDLINE, ScienceDirect, EMBASE. Jadad scale evaluated methodological quality of RCTs. Data on eradication rate were expressed as ITT. Relative risks (RR), pooled RR and 95% confidence intervals were calculated by Mantel-Haenszel. Data were entered into the RevMan 5.2 software (Nordic Cochrane Centre) using a random-effects model.

Comparison	RR: Relative Risk	Confidence Interval 95%	Difference in eradication rate	Number of enrolled patients
Sequential vs 10-day triple in LR areas	1.17	1.11–.23	12.1%	545 vs 556
Sequential vs 10-day triple in HR areas	1.14	0.97–1.33	7.3%	605 vs 621
Sequential vs 14-day triple in HR areas	1.04	0.95–1.13	0.7%	1256 vs 1252

Results: Databases identified 192 studies; 17 met inclusion criteria (5 new studies: 4 HRa and 1 LRa enclosed also Africa and North America: 749/4720 total patients). A comparison between sequential and 10-day triple therapy was available from both HRa and LRa, whilst sequential against 14-day triple data were coming only from HRa. Results are summarized in the table.

Conclusions: "Geographic weighting" could be the main factor affecting the lack of differences between sequential and 14-day triple therapy outcome.

Abstract no.: P11.10

HELICOBACTER PYLORI ERADICATION RATES WITH 10-DAY NON-BISMUTH QUADRUPLE THERAPY AND 10-DAY SEQUENTIAL THERAPY IN KOREA

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Background: Since the efficacy of the standard triple therapies for *Helicobacter pylori* (*H. pylori*) eradication has decreased, novel antibiotic regimens have been introduced. The aim of this study was to compare the efficacy of non-bismuth quadruple therapy with sequential therapy for the first-line *H. pylori* eradication in Korea.

Methods: One hundred and thirty-seven with proven *H. pylori* infection were randomly assigned to one of 2 regimens: amoxicillin 1000 mg with clarithromycin 500 mg, metronidazole 500 mg, and pantoprazole 40 mg twice daily for 10 days (non-bismuth quadruple therapy) or amoxicillin 1000 mg with pantoprazole 40 mg twice daily for 5 days followed by clarithromycin 500 mg with metronidazole 500 mg, and pantoprazole 40 mg twice daily for 5 days (sequential therapy). The success of *H. pylori* eradication was evaluated 4–5 weeks after completing treatment.

Results: Eradication rates were 93.4% in the concomitant therapy and 85% in the sequential therapy (per protocol), but the difference was not statistically significant (p = 0.154). Compliances were 97.2% in non-bismuth quadruple therapy and 97.1% in sequential therapy. Adverse events were generally mild in both groups.

Conclusions: Non-bismuth quadruple therapy led to a non-statistically advantage over sequential therapy, Two regimens are well tolerated and could be considered as the first-line empirical therapy for *H. pylori* in Korea.

Abstract no.: P11.11

NON-BISMUTH QUADRUPLE CONCOMITANT THERAPIES IN THE ERADICATION OF *HELICOBACTER PYLORI*: STANDARD VERSUS OPTIMIZED (14 DAYS, HIGH-DOSE PPI) REGIMENS IN CLINICAL PRACTICE

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Introduction: Non-bismuth quadruple "concomitant" regimen is increasingly used as first-line *H. pylori* eradication treatment.
Aims: To evaluate the efficacy and tolerability of the standard and optimized non-bismuth "concomitant" regimens.
Methods: Design: Prospective multicenter study. Patients: Consecutive *H. pylori*-infected patients. Treatment: In a first phase, patients received a standard concomitant therapy (CONC10): omeprazole 20 mg, amoxicillin 1 g, clarithromycin 500 mg and metronidazole 500 mg for 10 days b.i.d. In a second phase, patients received the same regimen but with esomeprazole 40 mg b.i.d. and lasting 14 days (CONC14+). Outcome: Eradication confirmed with 13C-urea breath test 4–8 weeks after therapy. Compliance/tolerance: Compliance and adverse events were determined through questioning and recovery of empty medication envelopes.
Results: 827 consecutive patients were included (mean age 48 years, 46% males, 21% peptic ulcer): 356 in CONC10 and 471 in CONC14+. Compliance with treatment was 94% and 95% respectively (non-statistically significant differences). Per-protocol eradication rates with CONC10 and CONC14+ were 86% (95% CI = 83–91%) and 93% (91–96%) ($p < 0.01$). Respective intention-to-treat cure rates were 86% (83–90%) and 91% (90–92%) ($p < 0.01$). Adverse effects (mostly mild) were reported in 32% of patients in CONC10 and in 44% in CONC14+ ($p < 0.05$), the most common being metallic taste, diarrhoea, nausea and abdominal pain.
Conclusion: An optimized (fourteen-day and high-dose esomeprazole) non-bismuth quadruple "concomitant" regimen for the eradication of *H. pylori* is more effective than the standard one, and achieves over 90% cure rate. Although the incidence of adverse events is higher with the optimized treatment, these are mostly mild, and do not negatively impact the compliance.

Abstract no.: P11.12

FOURTH-LINE RESCUE THERAPY WITH RIFABUTIN IN PATIENTS WITH THREE *H. PYLORI* ERADICATION FAILURES

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Background: In some cases, *H. pylori* infection persists even after 3 eradication treatments.
Aim: To evaluate the efficacy of an empirical forth-line rescue regimen with rifabutin in patients with 3 eradication failures, extending the experience of an ongoing multicenter study.
Methods: Design: Multicenter, prospective study. Patients: In whom the following 3 eradication treatments had consecutively failed:1st treatment: PPI+clarithromycin+amoxicillin; 2nd treatment:quadruple therapy(PPI+bismuth+tetracycline+metronidazole); 3rd treatment: PPI+amoxicillin+levofloxacin. Intervention: In patients failing these 3 regimens, a 4th regimen with rifabutin (150 mg b.i.d.), amoxicillin (1 g b.i.d.) and a PPI (standard dose b.i.d.) was prescribed for 10 days. Outcome: Eradication by 13C-urea breath test 4–8 weeks after therapy. Compliance and tolerance: Compliance was determined through questioning and recovery of empty medication envelopes. Incidence of adverse effects was evaluated by means of a questionnaire.
Results: 179 patients (mean age 50 years, 39% males, 22% peptic ulcer/78% functional or non-investigated dyspepsia) were included. Compliance: 11 patients did not take correctly the medication (in 10 cases due to adverse effects). Per-protocol and intention-to-treat eradication rates were 54.4% (95% CI = 47–62%) and 53.6% (46–61%). Adverse effects were reported in 56 (31%) patients, the most frequent being: nausea/vomiting, asthenia/anorexia, abdominal pain, diarrhea, fever, metallic taste, myalgia, hypertransaminasemia, leucopoenia (<1500 neutrophils, 5 cases), thrombopoenia (<150 000 platelets, 3 cases), headache, and aphthous stomatitis. Adverse effects were severe in two patients (vomiting). Myelotoxicity resolved spontaneously in all cases after finalizing the treatment.
Conclusion: Even after 3 previous *H. pylori* eradication failures, an empirical fourth-line rescue treatment with rifabutin may be effective in approximately 50% of the cases. Therefore, rifabutin-based rescue therapy constitutes a valid strategy after multiple previous eradication failures with key antibiotics such as amoxicillin, clarithromycin, metronidazole, tetracycline, and levofloxacin.

Abstract no.: P11.13

OPTIMIZED EMPIRIC TRIPLE AND CONCOMITANT THERAPY FOR *HELICOBACTER PYLORI* ERADICATION IN CLINICAL PRACTICE: THE OPTRICON STUDY

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Background and Aim: Empiric triple therapy for *H. pylori* infection should be abandoned when clarithromycin resistance rate is >15–20%. Whether a switch to a non-bismuth quadruple concomitant therapy can improve eradication rates in clinical practice is unknown. We aimed to compare the effectiveness and safety of two optimized triple (OPT-TRI) and concomitant (OPT-CON) therapies.
Methods: Prospective multicenter study in 16 Spanish centers, which prescribed triple therapy in clinical practice. In a first 3-month phase, patients received an OPT-TRI therapy, defined by esomeprazole (40 mg bid), amoxicillin (1 g bid) and clarithromycin (500 mg bid) for 14 days. Over the second 3-month phase, patients received an OPT-CON treatment, which consisted of an OPT-TRI therapy plus metronidazole (500 mg bid).
Results: 658 consecutive patients were included (360 OPT-TRI, 298 OPT-CON). An OPT-CON therapy achieved significantly higher eradication rates in the per protocol (83% [79–88%] and 93.7% [89–96%] [$p = 0.003$]) and intention-to-treat analysis (82.6% [95% CI = 79–87%) and 91.2% [88–96%], $p = 0.008$). Adverse events, mostly mild, were significantly more common with an OPT-CON therapy (42% vs 61%, $p < 0.001$), but compliance with therapy was similar between groups (92% vs 91.8, p 0.78. The rate of unacceptably low (<80%) (OPT-TRI 41% vs OPT-CON 14%) and good (>90%) cure rates (OPT-TRI 35% vs OPT-CON 65%) differed among participating centers.
Conclusion: An empiric OPT-CON therapy achieved significantly higher cure rates (>90%) compared to an OPT-TRI therapy. Addition of metronidazole to an OPT-TRI therapy increased eradication rates by 10%, resulting in a higher rate of adverse events but without impairing compliance with therapy.

Abstract no.: P11.14

SECOND-LINE RESCUE THERAPY WITH LEVOFLOXACIN AFTER FAILURE OF TREATMENT TO ERADICATE *HELICOBACTER PYLORI* INFECTION: TIME TRENDS IN A SPANISH MULTICENTER STUDY OF 1400 PATIENTS

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Background: Second-line bismuth-containing quadruple therapy is complex and frequently induces adverse effects. A triple rescue regimen containing levofloxacin is a potential alternative; however, resistance to quinolones is rapidly increasing.

Aim: To evaluate the efficacy and tolerability of a second-line triple regimen containing levofloxacin in patients whose *H. pylori* eradication treatment failed and to assess whether the efficacy of the regimen decreases with time.

Methods: Design: Prospective multicenter study. Patients: In whom PPI+clarithromycin+amoxicillin had failed. Intervention: Levofloxacin (500 mg b.i.d.)+amoxicillin (1 g b.i.d.)+PPI (standard dose b.i.d.) for 10 days. Outcome: Eradication confirmed by 13C-urea-breath test. Compliance&tolerance: Compliance was determined through questioning and recovery of empty medication envelopes. Incidence of adverse effects was evaluated by means of a questionnaire.

Results: 1400 consecutive patients were included (mean age 49 years, 49% males, 28% peptic ulcer/72% dyspepsia). 96% took all medications correctly. Per-protocol and intention-to-treat eradication rates were 74.6% (95% CI = 72–77%) and 73.4% (71–76%). Efficacy (intention-to-treat) was 76% in the year 2006, 68% in 2007, 70% in 2008, 76% in 2009, 73% in 2010, 71% in 2011, 75% in 2012, and 76% in 2013. In the multivariate analysis, none of the studied variables (including year of treatment) were associated with eradication success. Adverse effects were reported in 19% of patients, most commonly nausea, metallic taste, myalgia, abdominal pain, diarrhea and aphthous stomatitis. In 9 cases, the adverse effects were severe (nausea, metallic taste and myalgia), but none was serious.

Conclusion: Ten-day levofloxacin-containing therapy is an encouraging second-line strategy, providing a safe and simple alternative to quadruple therapy in patients whose previous standard triple therapy has failed. The efficacy of this regimen remains stable with time.

Abstract no.: P11.15

SYSTEMIC REVIEW AND META-ANALYSIS: IS A REGIMEN CONTAINING TETRACYCLINE AND AMOXICILLIN SUITABLE FOR *HELICOBACTER PYLORI* INFECTION?

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Objective: To conduct a systematic review and meta-analysis of clinical trials with treatment in one study arm including both tetracycline and amoxicillin for eradication of *Helicobacter pylori*.

Methods: Pubmed, Embase, Cochrane Central Register of Controlled Trials, Science Citation Index,China National Knowledge Infrastructure, Wanfang, and Chinese Biomedical Literature databases and abstract books of major European, American, and Asian gastroenterological meetings were searched. All clinical trials that examined the efficacy of *Helicobacter pylori* eradication therapies and included both tetracycline and amoxicillin in one study arm were selected for this systematic review and meta-analysis. Statistical analysis was performed with Comprehensive Meta-Analysis Software (Version 2).

Results: Thirty-three studies met the inclusion criteria. The pooled odds ratio (OR) was 0.90 (95% confidence interval: 0.42, 1.78) for quadruple therapy with amoxicillin and tetracycline versus other quadruple regimens, and total eradication rates were 78.1% by intention-to-treat (ITT) and 84.5% by per-protocol (PP) analyses in the experimental groups. The pooled eradication rates of 14-day quadruple regimens with a combination of amoxicillin and tetracycline were 82.3% by ITT and 89.0% by PP, and those of 10-day regimens were 84.6% by ITT and 93.7% by PP. ORs by ITT were 1.21 (95% CI: 0.64, 2.28) for triple regimens with amoxicillin and tetracycline versus other regimens and 1.81 (95% CI: 1.37, 2.41) for sequential treatment with amoxicillin and tetracycline versus other regimens, respectively.

Conclusions: Ten- or 14-day quadruple regimens with amoxicillin and tetracycline can achieve acceptable or good eradication rates and are suitable for the treatment of *Helicobacter pylori* infection.

Abstract no.: P11.16

THE EFFICACY AND SAFETY OF PROBIOTICS AS ADJUVANT AGENT FOR *HELICOBACTER PYLORI* INFECTION: AN META-ANALYSIS

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Aim: To determine whether probiotics could help to improve the eradication rates and reduce side effects, and to investigate the appropriate time, and duration to add the probiotics during anti-*H. pylori* treatment.

Methods: By searching Pubmed, Embase, the Cochrane Central Register of Controlled Trials, and the Science Citation Index, we selected for meta analysis all the randomized control trials (RCTs) comparing probiotics as an adjuvant agent of standard triple regimes with placebo or no treatment during anti-*H. pylori*. Statistical analysis was performed with the Comprehensive Meta Analysis Software (Version 2). Subgroup analyses were also carried out.

Results: Twenty-one RCTs involving a total of 3814 participants met the inclusion criteria. The pooled eradication rates of the probiotic group were 80.3% (1709/2128) by intention-to-treat (ITT) and 83.8% (1709/2039) by pro-protocol (PP), the pooled relative risk (RR) by ITT for probiotics supplementation versus without probiotics was 1.12 [95% confidence interval (CI): 1.06, 1.19]. There was also a reduced risk of overall *H. pylori* therapy-related adverse effects (RR = 0.60, 95% CI: 0.39, 0.92).

The subgroup analyses showed that the supplement before or after regimens all improved eradication rates for *H. pylori* infection. The more than 2 weeks duration of probiotic treatment made significant difference in efficacy.

Conclusions: Supplementation with probiotics for *H. pylori* eradication may be effective in increasing eradication rates and decreasing side effects. In addition, probiotics appear to have better effects on eradication rates in timing of before or after regimens, more than 2 weeks duration of probiotics administered appear to better eradication effectiveness.

Abstract no.: P11.17

COMPARISON OF THE EFFICACY OF 10 DAY-TRIPLE THERAPY-BASED, BISMUTH-CONTAINING QUADRUPLE THERAPY WITH SEQUENTIAL THERAPY AND CONCOMITANT THERAPY OF *HELICOBACTER PYLORI*

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Background/Aim: In recent studies of the first-line therapy, the eradication rate of sequential therapy is decreasing and as another option for *Helicobacter pylori* (HP) eradication, concomitant therapy and triple therapy-based, bismuth-containing quadruple therapy(TBQ) is tried. The aim of this study was to compare the efficacy of 10-day TBQ therapy with sequential therapy and concomitant nonbithmuth-based quadruple therapy for HP eradication.

Methods: From 2009 to 2014, 401 patients with HP infections allocated 3 groups. TBQ therapy group: lansoprazole (LPZ) 30 mg *bid,* Amoxicillin (AMX) 1000 mg *bid,* clarithromycin(CLA) 500 mg *bid,* metronidazole(MTZ) 500 mg *tid,* and tripotassiumdicitrato-bismuthate 600 mg *bid* for 10 days. Sequential therapy group: LPZ 30 mg *bid,* AMX 1000 mg *bid* for the first 5 days, followed LPZ

30 mg *bid*, CLA 500 mg *bid*, MTZ 500 mg *tid* for 5 days. Concomitant therapy group: PPI standard dose bid, AMX 500 mg tid, CLA 500 mg *bid*, metronidazole (MTZ) 500 mg *tid* for 1 week. The eradication of HP was assessed by urea breathing test and the side effects were assessed after 4 weeks.
Results: The eradication rate of TBQ therapy group was higher than sequential therapy group and concomitant therapy group in ITT analysis 85.3% (163/191) versus 73.7% (84/114) ($p = 0.009$) and 81/106(76.4%) ($p = 0.028$) and in PP analysis 85.3% (163/190) vs 75.0% (84/112) ($p = 0.015$) and 80.2% (81/101) ($p = 0.127$). There were no statistical differences in occurrence of side effects among three groups.
Conclusion: TBQ therapy for 10 days was effective to eradicate HP as first line therapy with mild and moderate side effects in Korea.

Abstract no.: P11.18

TREATMENT OF *HELICOBACTER PYLORI* INFECTION IN KOREA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background/Aims: The efficacy of 7-day standard triple therapy (STT), consisting of a proton pump inhibitor, clarithromycin, and amoxicillin for *Helicobacter pylori* has decreased over the past decade in Korea. This systemic review will give an overview of the trends of *H. pylori* eradication and present new therapeutic strategies in Korea.
Methods: An extensive bibliographical search of the literature concerning STT, sequential therapy (SET), quadruple therapy and various combinations of antibiotics in Korea was performed. All selected studies were randomized controlled trials (RCTs).
Results: Eighteen RCTs were eligible for systematic review. The alternative regimens comparing 7-day STT include: SET, concomitant therapy, levofloxacin-based therapy (LBT), bismuth-containing quadruple therapy (BCQT), and STT with prolonged treatment duration. The results of the meta-analysis for six studies concerning SET suggest that SET is superior to 7-day STT in terms of eradication rates. In the sub-analysis, however, there were no significant differences between SET and STT with prolonged treatment durations. There was only one RCT comparing BCQT and 7-day STT and it showed no significant differences in eradication rates. There were no significant differences between the effect of 7-day and 14-day STT based on two RCTs with regard to the duration of STT. Alternative regimens compared to 7-day BCQT as second-line therapy include: LBT, moxifloxacin-base therapy, and 14-day BCQT. The eradication rates of these alternative regimens as second-line therapies were not superior.
Conclusions: SET is superior to 7-day STT. However, 10-day STT and 14-day STT remain effective. BCQT as second-line therapy is still effective in Korea.

Abstract no.: P11.19

ERADICATION OF *HELICOBACTER PYLORI* INFECTION IN DIABETICS: META-ANALYSIS AND SYSTEMATIC REVIEW

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Background: Prevalence of *H. pylori* is decreasing in developed countries, while that of diabetes mellitus is increasing, resulting in a wide overlap of these conditions.
Aim: Meta-analysis and systematic review of the eradication results of *H. pylori* infection in Type 1 and Type 2 diabetes mellitus.
Data source: Pertinent data from Pubmed/Medline and UEGW, DDW and EHSG abstracts were extracted from 1983 to March 2014.
Methods: Comparative studies including diabetics and controls were included in meta-analysis using the fixed effect model. Systematic review included all similar treatment arms. Side effects were also assessed.
Results: Eight comparative and 6 pilot studies were suitable for analysis, including 815 diabetic patients and 412 controls. In comparative studies, the cumulative eradication rate in 654 diabetic cases was 60.5% (95% CI: 52.8–69.3) and 79.3% (68.1–91.3) in 451non-diabetic patients ($p = 0.03$) (OR: 1.78 (1.54–2.06). The rate of eradication was 63.8% (55.7-75.8) in Type 1 and 56.3% (46.2–65.4) in Type 2 diabetes ($p = 0.03$). On ITT basis, standard triple therapy was efficient in 67.8% (58.5–77.1) of diabetics, quadruple regimens achieved 77.3% (68.9–85.7), ranitidin bismuth citrate-based triple therapies 75.0% (66.4-83,6%). Sequential treatment was efficient in only 55.0% (45.1–64.2) The incidence of side effects was 32% in diabetics and 17% in controls ($p = 0.02$). However, significant heterogeneity between the studies was found.
Conclusion: Eradication rates of *H. pylori* infection are unacceptably low in diabetic patients, especially in Type 2 diabetes. Side effects were also more prevalent. Further controlled studies are necesssary to find optimal regimens in diabetics.

Abstract no.: P11.20

TRIPLE, SEQUENTIAL AND CONCOMITANT TREATMENT OF *HELICOBACTER PYLORI* INFECTION-PROSPECTIVE RANDOMIZED STUDY

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Background: *Helicobacter pylori* eradication rate with classic triple therapy is decreasing, new therapies should be tested before recommendation for new first line treatment is made.
Methods: Multicenter prospective randomised trial comparing esomeprazole 20 mg, amoxicillin 1000 mg, clarithromycin 500 mg bid for 7 days (EAC) with esomeprazole 20 mg, amoxicillin 1000 mg bid for 5 days and esomeprazole 20 mg, clarithromycin 500 mg, metronidazole 400 mg bid for 5 days (sequential) and esomeprazole 20 mg, amoxicillin 1000 mg, clarithromycin 500 mg and metronidazole 400 mg bid for 7 days (quadruple) were compared. *H. pylori* was diagnosed with RUT, histology, UBT and culture. Eradication was confirmed 1 month after therapy with UBT. We included 356 *H. pylori* treatment naive patients.
Results: Eradication rates (ITT) were 83.6% in EAC (116 patients); 94.2% in seguential (120 patients); 91.7% in quadruple (120 patients). Sequential therapy was superior to EAC ($p = 0.009$). *H. pylori* resistance rates were: metronidazole 25.9%, clarithromycin 10.5% and amoxicillin 0.6%. More clarithromycin and dual resistance (CM) strains were eradicated with sequential and quadruple therapies than with EAC ($p < 0.05$).There were no differences in indications for therapy, side effects, smoking or alcohol consumption between groups.
Conclusions: *H. pylori* eradication rate is significantly better with sequential treatment compared to EAC. Concomitant therapy was superior to EAC, but the difference did not reach significance.

Abstract no.: P11.21

NO SUPERIORITY OF LEVOFLOXACIN-CONTAINING SEQUENTIAL THERAPY IN ERADICATION OF *HELICOBACTER PYLORI* INFECTION IN KOREA

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Background/Aim: The eradication rates for *Helicobacter pylori* (*H. pylori*) have been declining and have reached an unacceptable level in Korea. This study was to compare the efficacy and the adverse effects of standard sequential therapy and levofloxacin-containing sequential therapy as first-line treatment for *H. pylori* eradication in Korea.
Methods: A total of 200 patients with proven *H. pylori* infection randomly received 10-day standard sequential (n = 100) or levofloxacin-containing sequential therapy (n = 100). The standard sequential group received rabeprazole 20 mg twice daily and amoxicillin 1 g twice daily for 5 days followed by rabeprazole 20 mg twice daily, clarithromycin 500 mg twice daily, and metronidazole 500 mg twice daily for five more days. The levofloxacin-containing sequential group was treated with rabeprazole 20 mg twice daily and amoxicillin 1 g twice daily for 5 days followed by rabeprazole 20 mg twice daily, levofloxacin 250 mg twice daily, and metronidazole 500 mg twice daily for five more days.
Results: Intention to treat eradication rates were 79.0% (95% CI: 70.0, 85.8%) and 78.0% (95% CI: 68.9, 85.0%) for standard sequential and levofloxacin-containing sequential groups, respectively ($p = .599$). Per protocol eradication rates were 84.0% (95% CI: 75.3, 90.1%) and 81.3% (95% CI: 72.3, 87.8%), respectively, for these two therapies ($p = .703$). There were no signifi-

cant between-group differences, in regard to the eradication rates, compliance, or side effects.
Conclusions: 10-day levofloxacin-containing sequential therapy regimen was not superior over standard sequential therapy regimen for the eradication of *H. pylori* in Korea.

Abstract no.: P11.22

SEQUENTIAL VERSUS CONCOMITANT TREATMENT AGAINST *H. PYLORI* STUDY IN A GREEK POPULATION

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Introduction: Maastricht consensus IV clearly suggests that countries with high clarithromycin and metronidazole resistance rates should use as first-line regiments against *H. pylori* either sequential or concomitant treatment.
Aim: Comparison of Sequential (ST) and Concomitant (CT) as first-line treatments against *H. pylori* in a prospective study of a Greek population.
Method: 212 patients (average age: 51.6 years), H.P (+), answered a preformed interview (history, habits, symptoms) and randomly received a 10-day eradication treatment either with:

1. ST:-PPIs × 2 plus:
   i. Amoxicillin 1 g × 2, for the first 5 days.
   ii. Clarithromycin 500 mg × 2 and Tinidazole 500 mg × 2 for the next 5 days [104 patients (M: 51, F: 53)].
2. CT:-PPIs × 2, Clarithromycin 500 mg × 2, Amoxicillin 1 g × 2 and Tinidazole 500 mg × 2 [108 patients (M: 39, F: 69)].

6–8 weeks after completing treatment all patients were controlled for eradication with UBT. Results were analyzed per-protocol (PP analysis) as well as with univariate logistic regression analysis (z test).
There is no statistical significance among the eradication percentages of ST and CT ($p = 0.587$).Of all parameters studied, none showed any statistically significant difference (sex and ex-smokers being at the cut-off).
Conlusion: The two regiments appear of equivalent value for Greek *H. pylori* positive patients.

Abstract no.: P11.23

SECOND-LINE RESCUE THERAPY WITH LEVOFLOXACIN AND BISMUTH AFTER FAILURE OF A *HELICOBACTER PYLORI* ERADICATION TREATMENT

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Background: The most commonly used second-line regimens for *H. pylori* eradication are bismuth-containing quadruple therapy and levofloxacin-containing triple therapy, both offering suboptimal results. Combining bismuth and levofloxacin in the same regimen may be an option as rescue regimen.
Aim: To evaluate the efficacy and tolerability of a second-line quadruple regimen containing levofloxacin and bismuth in patients whose previous *H. pylori* eradication treatment failed.
Methods: Design: Prospective multicenter study. Patients: In whom a standard triple therapy (PPI+clarithromycin+amoxicillin) or a non-bismuth quadruple therapy (PPI+clarithromycin+amoxicillin+metronidazole, either sequential or concomitant) had failed. Intervention: Esomeprazole (40 mg b.i.d.)+bismuth (240 mg b.i.d.)+levofloxacin (500 mg o.d.)+and amoxicillin (1 g b.i.d.) for 14 days. Outcome: Eradication was confirmed by ^{13}C-urea-breath-test. Compliance/tolerance: Compliance was determined through questioning and recovery of empty medication envelopes. Adverse effects were evaluated by means of a questionnaire.
Results: 78 patients were consecutively included. Mean age = 46 ± 16 years, 64% women, 14% peptic ulcer. Previous failed therapy included: standard-triple-therapy (57 patients), sequential(12), and concomitant (9). One patient did not return after treatment. 92% took all medications correctly. Per-protocol and intention-to-treat eradication rates were 89.5% (95% CI = 82–97%) and 87.2% (95% CI = 79–95%). Cure rates (per-protocol) were similar when compared depending on the diagnosis (peptic ulcer = 100% vs dyspepsia = 88%) and previous treatment (standard-triple-therapy = 89% vs sequential = 83% vs concomitant = 100%). Adverse effects were reported in 60% of patients (95% CI = 49–72%), most commonly nausea (27%), metallic taste (26%), diarrhoea (23%), and abdominal pain (22%). In 2 cases, the adverse effects (nausea) were severe (one patient discontinued the treatment), but none was serious.
Conclusion: 14-day bismuth- and levofloxacin-containing quadruple therapy is an effective and safe second-line strategy in patients whose previous standard-triple-therapy or non-bismuth quadruple(sequential or concomitant) therapy has failed, providing a simple and probably more effective alternative than bismuth-quadruple or levofloxacin-triple standard regimens.

Abstract no.: P11.24

EMPIRICAL RESCUE THERAPY AFTER *H. PYLORI* TREATMENT FAILURE. A 15 YEAR SINGLE CENTER STUDY OF 1000 PATIENTS

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Introduction: The most commonly used empirical therapies for *H. pylori* eradication fail up to 20–30% on first-line, and even more in "rescue" therapies, mainly due to increasing resistances and poor compliance.
Aims and Methods: To evaluate the efficacy of different "rescue" therapies empirically prescribed during 15-years to 1000 patients in whom at least one eradication regimen had failed. Design: Retrospective single-center study. Patients: 1000 consecutive rescue patients (1998–2013). Intervention: The most common eradication treatments were: (i) PPI-Amoxicillin-Levofloxacin (PPI-A-

	Eradicate +/−	Age	Sex	Smoke+	Smoke ex	NSAID	Alcohol	Gastric Ca	MALT	Dyspepsia
OR	1.27	1.01	1.7	0.96	1.9	1.51	2.23	2.47	0.96	1.05
SE	0.57	0.01	0.47	0.31	0.67	0.65	1.07	1.36	1.36	0.30
C.I.	0.52–3.1	0.99–1.02	0.98–2.94	0.51–1.81	0.95–3.79	0.64–3.54	0.87–5.72	0.84–7.29	0.05–15.5	0.6–1.86
p-value	0.587	0.21	0.058	0.91	0.068	0.33	0.094	0.1	0.97	0.84

	GERD	Gastric ulcer	Duodenal ulcer	Gastric atrophy	Intestinal metaplasia	Esophagitis	Side effects
OR	0.88	1.98	0.77	0.87	0.82	1.09	2.63
SE	0.24	1.42	0.29	0.42	0.38	0.41	1.32
C.I.	0.51–1.52	0.48–8.1	0.36–1.62	0.33–2.28	0.33–2.07	0.51–2.29	0.98–7.07
p -value	0.66	0.34	0.49	0.77	0.68	0.81	0.055

ST: PP = 88, 46%- CT: PP = 90.74%.

L), (ii) Ranitidine bismuth citrate-Tetracycline-Metronidazole (Rcb-T-M), (iii) Classic Quadruple therapy (PPI-Bismuth-Tetracycline-Metronidazole;PPI-B-T-M), (iv) Esomeprazole-Moxifloxacin-Amoxicillin (E-Mox-A), (v) PPI-Amoxicillin-Rifabutin (PPI-A-Rif). Rifabutin was prescribed only as 4th-line, and the other treatments were used both as 2nd and 3rd line. Regimens were prescribed empirically without retreating with the same drugs. Outcome: Eradication was defined as a negative 13C-UBT 4–8 weeks after treatment. Modified "intention-to-treat" analysis was used, considering patients with poor compliance, but not those who were lost during the follow-up.

Results: Overall eradication rates of *H. pylori* with 2nd, 3rd and 4th lines of "rescue" therapies were 75%, 71% and 50% respectively, with a cumulative eradication rate of 99.2%. The efficacy (and adverse effects) of treatments were 84% (24%) with E-Mox-A, 77% (24%) with PPI-L-A, 69% (22%) with PPI-B-T-M, 66% (33%) with Rcb-T-M, and 62% (38%) with PPI-A-Rif. The highest eradication was achieved with E-Moxi-A (83%) as 2nd-line treatment, regardless of the first-line regimen prescribed.

Conclusion: *H. pylori* eradication rates may reach 99% without performing bacterial culture by using a rescue strategy of 4 consecutive empirical treatments. The best rescue strategy to eradicate *H. pylori* is the consecutive administration of quinolones (2nd-line), PPI-B-T-M (3rd-line) and PPI-A-Rif (4th-line).

Abstract no.: P11.25

PEPTIC ULCER BLEEDING AND *HELICOBACTER PYLORI* ERADICATION – ARE WE FOLLOWING THE BEST STRATEGY IN CLINICAL PRACTICE?

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Background: *Helicobacter pylori* (Hp) prevalence is still very high in some European countries and this bacterium is the main responsible for peptic ulcer and its' complications.

Objective: Evaluate, in a tertiary hospital, what is the current strategy concerning Hp detection and eradication in patients with peptic ulcer bleeding (PUB).

Patients and Methods: One hundred and eighty one (males-64.6%; mean age-70.7 ± 16.4) consecutive patients admitted for PUB were retrospectively included. Ulcer location: duodenum-47.5%; stomach-45.9%; duodenum+stomach-5.5%; gastrojejunal anastomosis-1.1%. Other potential aetiologies, blood transfusion, endoscopic haemostasis, methods for Hp diagnosis, empiric Hp treatment and final results were registered.

Results: A significant number of patients were under antiplatelet agents (46.4%), non-steroidal anti-inflammatory drugs (37%) and anticoagulants (3.9%). Endoscopic haemostasis was performed in 65.2% and 71.3% received blood transfusions. Methods for Hp diagnosis were employed in 32% of patients, mainly by gastric biopsies. Empirical Hp treatment was initiated only in 12.7% and other 21% received indication to perform such treatment after discharge. Approximately 44.8% of patients were referred for a gastroenterology consultation and 3.9% died during hospitalization.

Conclusions: By now, Hp diagnosis and eradication for patients with PUB is not a priority in daily clinical practice, even in a tertiary hospital. This strategy is delayed for ambulatory follow-up and this could be a risk factor for non-compliance and early recurrence. In countries with high prevalence of Hp infection this strategy is probably inadequate and empirical treatment of Hp infection immediately after feeding is restarted is probably cost-effective.

Abstract no.: P11.26

PAN-EUROPEAN REGISTRY ON *H. PYLORI* MANAGEMENT *(HP-EUREG): SAFETY*

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Introduction: Antibacterial treatments often cause adverse events (AEs), especially when treatment contains two or more antibiotics.

Aims: To evaluate the AEs occurring during follow-up of patients registered at the Hp-EuReg.

Methods: The methodology applied was that established on Hp-EuReg project. AEs were registered using a pre-defined AE list for the typically reported AEs and with free text fields for uncommon AEs.

Results: Of the 3860 patients that have finished follow-up, 47% have shown at least one (26% of patients) or two (11%) AEs, although up to 7 or 8 different events occurred in some patients (1% and 0.2%, respectively). The most common AE was dysgeusia (metallic taste) in 9% of cases, followed by diarrhoea in 8%, nausea in 7%, and abdominal pain in 4%. Most AEs (62%) were mild and only 10% were of severe intensity; in any case, they only caused treatment discontinuation in 3.9% of patients. The average length of ARs was 6.7 days. Most common free text field AEs were headache (1.1%), candidiasis (oral 0.9%, vaginal 0.4%) and constipation (0.6%).

Conclusion: *H. pylori* eradication treatment cause adverse events in nearly half of the patients. However, the intensity is mostly mild and on average lasted less than a week. Adverse events only caused treatment discontinuation in 4% of the patients.

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SECOND-LINE *HELICOBACTER PYLORI* RESCUE THERAPY WITH MOXIFLOXACIN AFTER FAILURE OF STANDARD TRIPLE OR NON-BISMUTH QUADRUPLE TREATMENTS

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Background: Second-line bismuth-containing quadruple therapy is complex and frequently induces adverse effects. A triple rescue regimen containing moxifloxacin is a potential alternative.

Aim: To evaluate the efficacy and tolerability of a second-line triple regimen containing moxifloxacin in patients whose previous *Helicobacter pylori* eradication treatment failed.

Methods: Design: Prospective multicenter study. Patients: In whom a triple therapy or a non-bismuth-quadruple-therapy failed. Intervention: Moxifloxacin (400 mg o.d.), amoxicillin (1 g b.i.d.), and esomeprazole (40 mg b.i.d.) for 14 days. Outcome: Eradication confirmed by 13C-urea-breath-test. Compliance: Determined through questioning and recovery of empty medication envelopes. Tolerance: Evaluated by means of a questionnaire.

Results: 300 patients were consecutively included (mean age 49 ± 15 years, 58% women, 11% ulcer). Previous (failed) therapy: standard triple (68%), sequential (8%), and concomitant (24%). Ten patients did not return after

treatment. All but 8 patients (97%) took all medications. Per-protocol and intention-to-treat eradication rates were: 85.8% (95% CI = 82–90%) and 81.7 (95% CI = 77–86%). Cure rates were similar independently of diagnosis (ulcer = 79% vs dyspepsia = 82%) and previous treatment (standard triple = 82% vs sequential = 92% vs concomitant = 77%). In the multivariate analysis, age was the only variable associated with eradication (OR = 0.96; 95% CI = 0.94–0.98). Adverse effects were reported in 25% of patients: diarrhea (10%), abdominal pain (10%), and nausea (10%); 8% were severe but none was serious.

Conclusion: Fourteen-day moxifloxacin-containing therapy is an effective and safe second-line strategy in patients whose previous standard triple therapy or non-bismuth quadruple (sequential or concomitant) therapy has failed, providing a simple alternative to bismuth quadruple regimen.

Abstract no.: P11.28

EFFICACY OF *HELICOBACTER PYLORI* ERADICATION TREATMENT WITH MAINTENANCE OF ACID SECRETION FOR 24 HOURS

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Background: Insufficient inhibition of gastric acid during *Helicobacter pylori* treatment and bacterial resistance to antibiotics often causes eradication failure. Four-times-daily dosing (qid) of a PPI achieves pH >4.0 over 24 hours and mean 24-hours pH higher >6.0 during eradication, suggesting its potential utility as an optimal regimen for eradicating *H. pylori* infection. We reported that a tailored eradication with maintenance of acid inhibition based on antibiotic susceptibility had a high success rate. We aimed to compare eradication rate with tailored regimen based on antibiotic susceptibility and sitafloxacin (STFX)-based regimen.

Methods: In 200 *H. pylori*-positive Japanese patients, we compared the efficacy of two treatment strategies: a tailored strategy (n = 150), whereby patients infected with CAM-sensitive strain were treated with PPI (rabeprazole 10 mg, qid), amoxicillin (500 mg, qid), and CAM (200 mg, bid), with CAM-resistant administered the same doses of rabeprazole/amoxicillin and metronidazole (250 mg, bid) for 1 week. STFX-based regimen of rabeprazole/metronidazole and STFX (100 mg, bid) were selected (n = 50), irrespective with CAM-resistant.

Results: The intention-to-treat eradication rate in the tailored group was 98.0% (95% CI: 94.3–99.6%, 147/150), which was similar to that in STFX-based regimen (98.0% [89.4–99.9%, 49/50]). In the tailored treatment, the eradication rates for the CAM- and metronidazole-based treatments were similar (96.6% and 100%).

Conclusion: With maintaining acid secretion, not only a tailored eradication regimen based on CAM-susceptibility but also STFX-based regimen is useful. In addition, because STFX-based regimen can save the cost of CYP2C19 genotyping and culture tests, it may be more cost-effective than CYP2C19 genotype-based treatment.

Abstract no.: P11.29

THE COMPARISON OF *HELICOBACTER* ERADICATION RATES OF THREE REGIMENS: CONCOMITANT THERAPY VERSUS SEQUENTIAL THERAPY VERSUS STANDARD TRIPLE THERAPY

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Background: Currently, the *Helicobacter pylori* (*H. pylori*) eradication rate of clarithromycin-based triple therapy has decreased to an unacceptably low level, and novel therapeutic strategies are necessary.

Method: A total of 680 patients infected with *H. pylori* were divided into 4 groups, and each group was treated with a different eradication therapy. Clarithromycin-based triple therapy was applied to the first group (PAC group), whereas the second group was treated with metronidazole-based triple therapy (PAM group). The third group was treated with rabeprazole and amoxicillin, followed by rabeprazole, clarithromycin, and metronidazole (sequential group). The final group was simultaneously treated with rabeprazole, amoxicillin clarithromycin, and metronidazole (concomitant therapy group). In the case of a failure to eradicate *H. pylori,* second-line quadruple and third-line eradication therapies were administered.

Results: The eradication rates were 76.2% (109/143) in the PAC group, 84.2% (117/139) in the PAM group, 84.4% (119/141) in the sequential group, and 94.4% (135/143) in the concomitant group ($p = 0.0002$). The second-line therapy was applied to 90 patients, and the eradication rate was 84.4% (76/90). The eradication rate for the third-line therapy was 42.9% (6/14).

Conclusion: The eradication rate for the concomitant therapywas much higher than those of the standard triple therapy or sequential therapy.

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TEN-DAYS CONCOMITANT THERAPY IS SUPERIOR TO SEQUENTIAL THERAPY FOR *HELICOBACTER PYLORI* ERADICATION

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Because the efficacy of the standard triple therapy for *Helicobacter pylori* eradication has declined, new regimens such as sequential therapy (ST) and concomitant therapy (CoCTx) have been introduced. The aim of this study was to compare the efficacy of 10-days sequential therapy and 10-days CoCTx for *H. pylori* eradication.

We retrospectively reviewed the medical records of 316 patients with proven *H. pylori* infection. They were assigned to one of 2 regimens: (i) ST (n = 191): lansoprazole 30 mg and amoxacillin 1 g for 5 days followed by lansoprazole 30 mg, metronidazole 500 mg, and clarithromycin 500 mg for 5 days; (ii) CoCTx (n = 125): lansoprazole 30 mg, amoxicillin 1 g, metronidazole 500 mg, and clarithromycin 500 mg for 10 days. All drugs were administered twice a day. Bacterial eradication was checked by using a ^{13}C-urea breath test, at least 4 weeks after treatment.

The mean age and male to female ratio was 51.74 and 1.03. Baseline characteristics were not different in both groups. Ten day CoCTx group (94.4%, 118/125) showed better eradication rate than ST group (82.2%, 157/191) ($p = 0.002$). The difference was statistically significant. Drug compliances were not statistically different between both groups (ST: 96.3%, 184/191; CoCTx: 92.8%, 116/125) ($p = 0.19$). Side effects were more frequently reported in the CoCTx group (42.4%) than in the ST group (29.8%) ($p = 0.03$).

Ten-days CoCTx was superior to ST in terms of eradicating *H. pylori* infection. Although the CoCTx was producing more side effects than ST, CoCTx is thought to be a promising alternative to ST as a treatment regimen for *H. pylori* eradication.

Abstract no.: P11.31

FUSOGENIC LIPOSOMES AS PROMISING DELIVERY SYSTEMS AGAINST *HELICOBACTER PYLORI*

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As the antibiotic resistance of *Helicobacter pylori* increases so does the need to find alternatives ways to eradicate this bacterium. For example, glycopeptide antibiotics are not used against Gram-negative bacteria because these drugs act on the peptidoglycan, which is inaccessible to reach due the outer membrane present. To circumvent this limitation, fusogenic liposomes were tested to verify their ability to fuse with the outer membrane of *H. pylori* and to release their content into the periplasmic space, where the peptidoglycan is. Two formulations were developed using 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE) and cholesterol hemisuccinate (CHEMS) and other lipids in their composition. Liposomes were prepared by the dehydration-rehydration method followed by an extrusion step to obtain vesicles with a diameter below 200 nm. Two molecules were used in the present work, vancomycin and lysozyme that, in the free form, are not able to penetrate the Gram-negative bacteria membrane. They were loaded in liposomes and a microbiological assay in vitro to determine the minimum inhibitory concentrations (MIC) against Escherichia coli B, Campylobacter jejuni CCUG11284 and *H. pylori* strains B45 and 26695 was conducted. Free vancomycin and lysozyme were tested as controls. While lysozyme loaded in liposomes did not show a lower MIC over the free lysozyme, an advantage in terms of antibacterial effect was observed for vancomycin loaded liposomes. The inferior MIC value in comparison to the free

vancomycin is indicative that liposomes may be suitable for delivering drugs that by other ways would not be active against *H. pylori*. Supported by FCT project PTDC/EBB-EBI/119860/2010.

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COMPARISON OF *HELICOBACTER PYLORI* ERADICATION RATE AMONG CONCOMITANT, TAILORED, AND SEQUENTIAL THERAPY

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Background: Currently, the *Helicobacter pylori* eradication rate of clarithromycin-based triple therapy has decreased to an unacceptably low level, and novel therapeutic strategies are necessary.
Aim: To compare the eradication rates of concomitant, tailored, and sequential therapy.
Methods: A total 712 patients infected with *Helicobacter pylori* were divided into 3 groups, and each group was treated with a different eradication therapy. The first group was simultaneously treated with rabeprazole, amoxicillin clarithromycin, and metronidazole for 7 days (concomitant therapy group). A test for point mutations in the 23S rRNA gene was conducted in the second group (tailored therapy group) which was treated with amoxicillin, rabeprazole, and clarithromycin in the absence of resistence for 7 days, whereas clarithromycin was replaced by metronidazole if the resistence was detected. The final group was treated with rabeprazole and amoxicillin for 5 days, followed by rabeprazole, clarithromycin, and metronidazole for 5 days (sequential group).
Results: The eradication rates were 92.4% (194/210) in the concomitant group, 90.6% (193/213) in the tailored group ($p = 0.514$), and 84.6% (176/208) in the sequential group ($p = 0.012$).
Conclusion: The eradication rates for concomitant and tailored therapy were similar. And both were higher than sequential therapy.

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COMPARISON OF 10-DAY SEQUENTIAL THERAPY WITH BISMUTH BASED QUADRUPLE THERAPY FOR SECOND LINE *HELICOBACTER PYLORI* ERADICATION

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Background: 10-day sequential therapy has been evaluated as the first line therapy for *Helicobacter pylori* eradication and studies of sequential therapy as a second line therapy has been scarce. The aim of our study was to evaluate the efficacy of 10-day sequential therapy as second line treatment after failure of standard triple therapy.
Method: Patients diagnosed as *H. pylori* infection by rapid urease test, giemsa staining, or 13C-urea breath test and who failed from standard triple therapy for *H. pylori* eradication from January, 2010 to June, 2013 in Yeungnam university hospital were included. Post treatment *H. pylori* status was determined by rapid urease test, giemsa staining, or 13C-urea breath test. Eradication rate, side effects were compared.
Results: A total of 123 *H. pylori* infected patients were included and 39 patients were treated by bismuth based quadruple therapy and 84 patients, by 10-day sequential therapy. Age and sex were not significantly different between both groups. The per-protocol eradication rates were 82.1% (32/39) in quadruple group and 60.7% (51/84) in sequential group. Side effects were similar in both groups (quadruple group, 20.5% vs sequential group, 11.9%, $p = 0.273$).
Conclusion: For second line *H. pylori* eradication after failure of standard triple therapy, bismuth based quadruple therapy showed significantly higher *H. pylori* eradication rate than 10-day sequential therapy. Further prospective studies are needed to evaluate efficacy of 10-day sequential therapy as second line *H. pylori* eradication treatment.

Abstract no.: P11.34

THE EFFECT OF *H. PYLORI* ERADICATION ON THE THERAPY OF REFLUX ESOPHAGITIS_A MULTI-CENTER RANDOMIZED CONTROL STUDY

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Aims: To explore the effect of *H. pylori* and *H. pylori* eradication on the therapy of reflux esophagitis.
Methods: Patients with reflux symptoms and diagnosed as reflux esophagitis by endoscopy were enrolled. Based on the results of rapid urease test and WS stain, the patients were divided into *H. pylori* positive and *H. pylori* negative group. *H. pylori* positive patients were randomly given *H. pylori* eradication treatment for 10 days, then Esomeprazole 20 mg bid for 46 days. Other patients underwent Esomeprazole 20 mg bid therapy for 8 weeks. After 8 weeks of treatment, all patients underwent gastroscopy again. For patients who underwent *H. pylori* eradication, negative WS stain means successful eradication. Then the patients were divided into three groups: *H. pylori* positive eradicated, *H. pylori* positive uneradicated (patients without *H. pylori* eradicaiton or unsuccessful eradication) and *H. pylori* negative. Before and after therapy, the reflux symptoms were scored and compared. Healing rate of each group was compared.
Results: (i) There were 176 *H. pylori* positive and 180 *H. pylori* negative cases. For *H. pylori* positive patients, 92 cases were eradicated. (ii) The healing rates of esophagitis in *H. pylori* positive eradicanted group and *H. pylori* positive uneradicated group reached 80.4% and 79.8% respectively, ($p = 0.911$). The scores of reflux symptoms were 0.22 and 0.14 respectively, ($p = 0.588$).(3) The healing rates of esophagitis in *H. pylori* positive uneradicated group and *H. pylori* negative group were 79.8% and 82.2% respectively, ($p = 0.848$).The scores of reflux symptoms were 0.14 and 0.21 respectively, ($p = 0.546$).
Conclusions: On the basis of Esomaprazole therapy for 8 week, *H. pylori* infection and *H. pylori* eradication have no significant effect on the therapy of reflux esophagitis.

Abstract no.: P11.35

SECOND-LINE REGIMEN'S EFFICACY AGAINST *HELICOBACTER PYLORI* INFECTION AFTER STANDARD TRIPLE THERAPY WITH PPI, AMOXICILLIN & CLARITHROMYCIN: META-ANALYSES

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Background: *Helicobacter pylori* infection is usually treated with a proton pump inhibitor (PPI), amoxicillin and clarithromycin, but it fails in ≥20% of patients.
Aim: To estimate, by a systematic review and meta-analyses, the most effective rescue treatments after the failure of a first-line clarithromycin-amoxicillin-PPI therapy.
Methods: *Selection of studies:* Meta-analyses were performed with randomized clinical trials that assessed the efficacy of second-line regimens; the generic inverse variance was applied on prospective and retrospective studies. *Inclusion criteria:* Studies treating *H. pylori*-positive patients after clarithromycin-amoxicillin-PPI failure. *Exclusion criteria:* Second-line treatment based on the antibiotic sensitivity, or if the confirmation of eradication was made only by serology, PCR or polyclonal stool antigen test. *Search strategy:* Bibliographical searches were performed in PubMed, CINAHL, Cochrane Library, ClinicalTrials.gov, and several international congresses, up to May 2014. *Data synthesis:* Intention-to-treat eradication rate.
Results: The efficacies of the second-line treatments are shown in the table attached. A meta-analysis comparing the triple therapy with levofloxacin-amoxicillin-PPI against the quadruple bismuth-metronidazole-tetracycline-PPI regimen showed a non-statistically significant tendency towards better results with levofloxacin (OR = 1.62; 95% CI = 0.84–3.14; $p = 0.15$; $I^2 = 75\%$; 7 studies; 1158 patients).
Conclusion: The most effective second-line treatments, after a clarithromycin-amoxicillin-PPI failure, are the metronidazole-amoxicillin-PPI or a 10 day levofloxacin-amoxicillin-PPI therapy. More high quality trials, performed outside Japan, are needed to verify the efficacy of the 14 day dual therapy with amoxicillin-PPI.

Second-line treatment	E.R.	N.S.	N.P.	95% C.I.	I^2
Levofloxacin + Amoxicillin + PPI					
Overall	75%	21	2919	70–80%	88%
7 day treatment	69%	11	632	64–74%	53%
10 day treatment	83%	11	1946	77–89%	89%
10 days with L (500 mg/24 hours) + A(1 g/12 hours)+PPI	87%	7	373	81–94%	77%
*Removing 1 outlier study	92%	6	273	89–95%	0%
14 day treatment	74%	3	341	70–78%	96%
*Removing 1 outlier study	86%	2	151	81–92%	0%
Bismuth + Metronidazole + Tetracycline + PPI					
Overall	77%	43	3685	74–81%	86%
7 day treatment	75%	31	2345	71–80%	84%
10 day treatment	77%	2	142	60–93%	76%
14 day treatment	81%	15	1187	76–86%	83%
Metronidazole + Amoxicillin + PPI					
Overall	88%	24	1642	85–91%	75%
7 day treatment	75%	24	1160	85–91%	75%
7 days with M (250 mg/12 hour) + A(750 mg/12 hours)+PPI	92%	12	751	89–95%	48%
10 day treatment	84%	4	314	77–91%	69%
14 day treatment	81%	2	127	75–88%	0%
Amoxicillin + PPI (14 days – all the studies were done in Japan)					
Overall	82%	5	200	69–95%	87%
14 day with A (500 mg/6 hours) + PPI(10 mg/6 hours)	93%	3	106	88–98%	3%
14 day with A (1 g/12 hours) + PPI (20 mg/12 hours)	66%	2	94	51–81%	58%

E.R., eradication rate; N.S., Number of studies; N.P., number of patients.

Abstract no.: P11.36

RECOVERY OF GASTRIC FUNCTION AFTER ACETIUM ADMINISTRATION: A 6 MONTHS STUDY IN CHRONIC ATROPHIC GASTRITIS SUBJECTS

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Background: No consensus from different studies exists regarding the reversibility of atrophic gastritis; however, removal of *H. pylori* from the already atrophic stomach may block further progression of the disease. Recently a new compound (L-cystein Acetium, Biohit, Finland) has been proposed for prevention of gastric carcinogenesis in patients with atrophic gastritis.
Aims: To assess the changes in gastric function after long term administration of L-cysteine in moderate to severe atrophic gastritis.
Methods: 30 patients with histological features of moderate-severe body atrophic gastritis and sPGI <25 μg/L (7 men, mean age 47.9 years, range 27–71) had sPGI and sG17 measured at baseline. In 8 patients autoimmune origin was confirmed by anti-parietal cell antibodies, the rest underwent eradication therapy for *Helicobacter pylori* infection earlier. Long term oral therapy with Acetium (3 × 100 mg L-cysteine/day before meals) has been initiated and serologic markers were determined at 3 and/or 6 months.
Results: Mean sPGI levels prior to treatment were 7.9 μg/L, compared to the latest measurements' mean of 11.1 μg/L ($p < 0.001$) reflecting possible increase in active parietal cell mass. On the other hand the mean baseline level of sG17 decreased from 34.4 pmol/L to 26.71 pmol/L ($p < 0.001$) indicating changes in the negative feedback of the regulation transmitted by gastrin.
Conclusions: L-cysteine seems to be useful in restoring gastric secretion in subjects with chronic atrophic gastritis both after H.p. eradication and in case of autoimmune etiology.

Abstract no.: P11.37

BROCCOLI SPROUT EXTRACT CONTAINING SULFORAPHANE (BSES) CAN PREVENT LIPID PEROXIDATION IN THE GASTRIC MUCOSA WITH *HELICOBACTER PYLORI* INFECTION

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Background/Aims: The standard triple therapy for *Helicobacter pylori* eradication has become less effective, requiring the development of new treatment strategies that increase the eradication rate and reduce adverse effects. A broccoli sprout extract containing sulforaphane (BSES) exhibits anti-oxidative and bactericidal activity against *H. pylori*. The aims of this study were to investigate whether BSES inhibits *H. pylori* infection density and exerts an anti-oxidative effect on gastric mucosal damage.
Methods: The enrolled subjects were randomized double blindly into three groups. Finally, 33 *H. pylori* (+) BSES treatment subjects (group A), 28 *H. pylori* (+) placebo subjects (group B), and 28 *H. pylori* (−) BSES treatment subjects (group C) were studied. *H. pylori* infection density was quantified indirectly by a C^{13}-urea breath test (UBT) and measurement of the ammonia concentration in gastric juice aspirate through the gastroscopic examination. Malondialdehyde (MDA), as an oxidative damage biomarker, and reduced glutathione (GSH), as an anti-oxidant biomarker, were measured in gastric mucosa by ELISA.
Results: BSES treatment did not significantly affect UBT values or gastric juice ammonia concentration in Group A, respectively ($p = 0.634$, $p = 0.505$). BSES treatment did significantly reduce mucosal MDA concentrations in Group A ($p < 0.05$) and Group C ($p < 0.001$), while gastric mucosal GSH concentrations were not different before and after treatment in all three groups.
Conclusions: BSES did not inhibit *H. pylori* infection density in the stomach. However, BSES prevented lipid peroxidation in the gastric mucosa and may play a cytoprotective role in *H. pylori*-induced gastritis.

Abstract no.: P11.38

THE EFFECT OF MOXIFLOXACIN CONTAINING TRIPLE THERAPY AS SECOND-LINE TREATMENT FOR *HELICOBACTER PYLORI* ERADICATION INFECTION

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Background and Aim: The aim of this study was to investigate the value of triple therapy with rabeprazole, moxifloxacin, and amoxicillin in second-line treatment and the impact of treatment duration on eradication success.
Method: Between 2011 and 2013, 133 patients who had failed first-line proton pump inhibitor-based triple therapy were randomized to oral rabeprazole (20 mg b.i.d.), axoxicillin (1000 mg b.i.d.), and moxifloxacin (400 mg q.d.) for either 7 (RAM-7 group, n = 52) or 14 days (RAM-14 group, n = 81). The eradication was compared by confirming of eradication rate. *H. pylori* status was evaluated by histologic finding, Campylobacter-like organism test and ^{13}C urea breath test.
Result: The eradication rates by intention-to-treat analysis were 69.2% (36/52) and 81.4% (66/81) in the RAM-7 group and the RAM-14 group, respectively ($p = 0.031$). The eradication rates by per-protocol analysis after excluding 8.4% of patients who were lost to follow-up were 73.5% (36/49) and 90.4% (66/73) in the RAM-7 group and the RAM-14 group, respectively ($p = 0.013$). Compliance was very good in the both groups (100%). The adverse event rates were 26.5% (13/49) and 20.5% (15/73) in the RAM-7 group and the RAM-14 group, respectively ($p = 0.441$). There was no significant difference in the 1st-line treatment, previous ulcer history, smoking, alcohol, and endoscopic finding between RAM-7 and RAM-14 group.
Conclusion: Second-line *H. pylori* eradication therapy with rabeprazole, amoxicillin, and moxifloxacin is very effective and well tolerated. Fourteen days of treatment significantly increase the eradication rate.

Abstract no.: P11.39

EFFICACY OF A SECOND-LINE LEVOFLOXACIN-CONTAINING TRIPLE THERAPY AFTER THE FAILURE OF THE NON-BISMUTH SEQUENTIAL OR CONCOMITANT TREATMENTS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: *Helicobacter pylori* infection is frequently treated with non-bismuth quadruple therapies (named "sequential" and "concomitant" regimens), but little is known about the management of treatment failures.

Aim: To investigate, by systematic review and meta-analyses, the efficacy of a levofloxacin, amoxicillin and a proton pump inhibitor (PPI) treatment, after failure of the sequential or concomitant regimens.
Methods: Selection of studies: The generic inverse variance was applied on studies evaluating the efficacy of a second-line levofloxacin-amoxicillin-PPI regimen after the sequential (a first treatment phase with amoxicillin-PPI, followed by a second phase with clarithromycin-nitroimidazole-PPI) or concomitant (the same drugs used in the sequential treatment, but all given concomitantly) first-line failure. Exclusion criteria: Second-line treatment based on the antibiotic sensitivity. Search strategy: Bibliographical searches were performed in PubMed, CINAHL, Cochrane Library, ClinicalTrials.gov, and several international congresses, up to May 2014. Data synthesis: Intention-to-treat eradication rate.
Results: The eradication rate of a 10-day levofloxacin-amoxicillin-PPI therapy after the concomitant and sequential treatment failure was, respectively, 78% (95% CI = 58–97%; I^2 = 67%; 3 studies; 86 patients) and 81% (95% CI = 73–90%; I^2 = 19%; 6 studies; 107 patients). After the sequential treatment, all studies but one gave 250 mg b.i.d. of levofloxacin.
Conclusion: A 10-day second-line regimen with levofloxacin-amoxicillin-PPI is effective after the failure of the sequential or concomitant treatments, achieving approximately an 80% eradication rate.

Abstract no.: P11.40

CAN PROBIOTICS (*BACILLUS SUBTILIS, STREPTOCOCCUS FAECIUM* STRAIN) INCREASE THE SUCCESSFUL ERADICATION OF *HELICOBACTER PYLORI* INFECTION IN KOREA?

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Background/Aims: This study was performed to evaluate whether the addition of probiotics to proton pump inhibitor-based triple therapy increases the likelihood of successful *Helicobacter pylori (H. pylori)* eradication.
Methods: We retrospectively reviewed 218 patients who undertaken *H. pylori* eradication therapy between March 2010 and February 2012. These patients were classified three groups, (A) PPI-based 7-day triple therapy, (B) the same triple therapy plus probiotics for 7-day, and (C) the same triple therapy plus probiotics for 14-day. We compared eradication rates of three group. ^{13}C-urea breath test was performed at 4 weeks after completion of the therapy to confirm the successful eradication.
Results: The total eradication rate of these patients was 71.1% (155/218). By per protocol analysis, *H. pylori* eradication rates for the groups A, B, and C were 64.4% (67/104), 80.8% (42/52), and 74.2% (46/62) respectively (p = 0.086). The eradication rate of the group B was significantly higher than that of the group A (p = 0.036). In subgroup analysis, *H. pylori* eradication rate of the probiotics group (B and C) was 77.2% (88/114), which was significantly higher than that of the non-probiotics group (A) (p = 0.038). Regardless of adding probiotics, the eradication rate of group C which was treated for 14 days was not significantly higher than that of group A and B which was treated for 7 days (74.2% vs 69.9%, p = 0.525).
Conclusions: The addition of probiotics to conventional triple therapy increases the eradication rate of *H. pylori* in this study, regardless of duration of eradication treatment.

Abstract no.: P11.41
This abstract has been withdrawn.

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Abstract no.: P11.43

EFFICACY OF MODIFIED TRIPLE THERAPY WITH BISMUTH SUBSTRATE AS FIRST-LINE THERAPY TO ERADICATE *H. PYLORI* IN SAINT-PETERSBURG POPULATION

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Background: The high rate of *H. pylori* resistance to clarithromycin in St. Petersburg (Russia), the insufficient efficacy of standard triple therapy make it necessary to perform this study.
Objective: The aim of this study was to assess efficacy of a modified triple therapy with bismuth substrate, as first-line treatment in the eradication of *H. pylori* infection in population of high clarithromycin resistance.
Methods: A total of 40 outpatients with *H. pylori*-associated diseases as documented by the rapid urease test (RUT), culture or polymerase chain reaction (PCR) were treated with the modified triple therapy with bismuth substrate: rabeprazole (40 mg/q12 hours), clarithromycin (500 mg/q12 hours), amoxicillin (1000 mg/q12 hours), bismuth subcitrate (240 mg tablets/q12 hours) for 10 days. Eradication was confirmed by a 13C-urea breath test or monoclonal stool antigen test 4-8 weeks after therapy. Compliance was determined through questioning and recovery of empty medication envelopes. Incidence of adverse effects was evaluated by means of a questionnaire.
Results: 40 outpatients (mean age 43 ± 13, 75% females, 37.5% peptic ulcer/62.5% dyspepsia) initially included and two were lost to follow-up. Four patients (10.5%) did not complete treatment due to adverse events (all have moderate diarrhea, 3 of them - nausea). Per-protocol and intention-to-treat eradication rates were 97% (95% CI, 88–100%) and 87% (78–96%). Adverse effects were reported in 29% of patients, the most common were a bitter taste (18%), diarrhea (18%) and nausea (10.5%).
Conclusion: Ten-day modified triple therapy with bismuth substrate achieves a high eradication rate in patients with *H. pylori* infection in population of high clarithromycin resistance.

Abstract no.: P11.44

Hp RESCUE THERAPY AFTER FOUR PREVIOUS FAILURES: AN EMPIRICAL 5 WEEKS SCHEDULE OF TREATMENT

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Background: *H. pylori* is the most common chronic bacterial infection in humans. Thus eradication therapy is both an important curative and preventative measure. There are currently only anecdotal reports after the failure of four eradication attempts with different regimens. We propose a 5 week fifth line treatment comprising of antibiotics, PPI, lactoferrin, acetyl-cysteine and lactobacilli rhamnosus in case of the failure of both standard triple and sequential therapies.
Methods and Results: The above mentioned treatment has been applied as a fifth attempt after failure of both standard triple, sequential therapies and alternate regimens using a different combination of antibiotics in the case of 30 patients (16 male), aged 41–71 (mean 60) years, in the Veneto region, Northern Italy with a success rate of 73.3% per protocol analysis. Eradication has been confirmed by urea breath test. No cultures with antibiotic sensitivity testing were done. All patients completed treatment with only few minor side-effects (abdominal or epigastric pain, diarrhea). Our treatment schedule based on amoxicillin and levofloxacin had a success rate of 73.3%, and we achieved eradication also in cases where previous levofloxacin-based regimens and sequential treatments failed.
Conclusions: After several failed eradication attempts the mentioned regimen seems to be promising with an accettable success rate. The complexity of the regimen which consists of six different drugs administered for 5 weeks raises patient compliance issues which may adversely influence the outcome.

Abstract no.: P11.45

WHEN IS THE BEST TIME TO ADMINISTER MEDICATION FOR *H. PYLORI* ERADICATION?

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Background and Aim: The combination therapy of lansoprazole, amoxicillin, and clarithromycin (LAC regimen) is one of the most effective eradication regimen of *Helicobacter pylori* positive ulcer patients, but it has not been studied well that when is the most effective time to administer for eradication.
Methods: From January 2010 to December 2013, we reviewed a total 391 patients with *H. pylori* infection. 85 patients (Group A) with *H. pylori* infection received with LAC regimen (lansoplazole 30 mg bid, amoxicillin 1.0 g bid, clarithromycin 500 mg bid.) at 30 min before breakfast and dinner for 1 week. Another 165 patients (Group B) received with LAC regimen immediately after a meal and the other 141 patients (Group C) at 30 min after breakfast and din-

ner. After the 7 day treatment period, the patients did not receive any further treatment. After 5–6 weeks urea breath test was performed for checking *H. pylori* eradication.
Results: 60 patients (15.34%) were diagnosed with gastric ulcer, 231 patients (59.07%) with duodenal ulcer and the remaining 100 were those who with a family history of stomach cancer or who wanted an eradication of *H. pylori*. The total *H. pylori* eradication rate was 74.2% (Cl 95%: 69.81-88.53%). The eradication rates were 74.12% (63/85) in the group A, 70.91% (117/165) in the group B and 78.01% (112/141) in the group C. There was no statistical significant difference between three groups ($p = 0.369$).
Conclusions: Timing of administration of LAC regimen did not significantly influence *H. pylori* eradication rates.

Abstract no.: P11.46

STANDARD TRIPLE THERAPY FOR *HELICOBACTER PYLORI* INFECTION IN CHINA: A META-ANALYSIS

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Aim: To assess the efficacy and safety of standard triple therapy compared to other pre-existing and new therapies in China.
Methods: Literature searches were conducted in the following databases: PubMed, Embase, the Cochrane Central Register of Controlled Trials, the VIP database, the China National Knowledge Infrastructure database (CNKI), and the Chinese Biomedical Database (CBM). A meta-analysis of all randomized controlled trials (RCTs) comparing standard triple therapy for the eradication of *Helicobacter pylori* (*H. pylori*) with pre-existing and new therapies in China was performed using Comprehensive Meta-Analysis (CMA) 2.0. The Mantel-Haenszel method was used for pooling dichotomous data. We also conducted subgroup analyses according to age, duration of treatment and drug type. Sensitivity analyses and cumulative meta-analysis were also performed with CMA 2.0.
Results: A total of 49 RCTs including 8332 patients were assessed. This meta-analysis showed that standard triple therapy with proton pump inhibitors (PPIs), amoxicillin (AMO) and clarithromycin (CLA) was inferior to sequenti¬al therapy [relative risk (RR) = 0.863; 95% confidence interval (CI): 0.824–0.904], but was not superior to quadruple therapy (RR = 1.073; 95% CI: 0.849–1.357) or other triple therapies (RR = 1.01; 95% CI: 0.936–1.089). The meta-analysis also suggested that standard triple therapy is slightly more effective than dual therapy (RR = 1.14; 95% CI: 0.99–1.31).
Conclusion: The eradication rates with a standard triple therapy consisting of PPI, AMO, and CLA are suboptimal in China, and new treatment agents need to be developed.

Abstract no.: P11.47

TRIPLE VERSUS SEQUENTIAL MOXIFLOXACINE BASED THERAPY FOR *HELICOBACTER PYLORI* ERADICATION-A RANDOMISED CLINICAL TRIAL

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Introduction: Since clarithromycin resistance is increasing, we compare non-bismuth, moxifloxacine-based quadriple sequential versus concomitant eradication therapy for *Helicobacter pylori* eradication.
Aim and Methods: A total of 65 patients, naïve to eradication therapy with peptic ulcer disease or dyspepsia were randomly assigned into two groups. The first group (n = 33) received pantoprazole 40 mg bid and amoxycillin 1 g bid during 5 days followed by 5 days of pantoprazole 40 mg bid, moxifloxacine 400 mg/day and metronidazole 500 mg bid (sequential). The other group (n = 32) received pantoprazole 40 mg bid, amoxycillin 1 g bid, and moxifloxacine 400 mg/day during the 10 days (triple therapy). The success of *Helicobacter pylori* was assessed with the (13) C-urea breath or histology 6 weeks after the therapy.
Results: 59 patients (91%) completed the study. Sequential and triple eradication rates were 85% (28/33) versus 84% (27/32) by intention to treat (p = n.s) and 96% (28/29) versus 90% (27/30) (p = n.s) per protocol analyses, respectively. Mild adverse events were more frequently reported in the concomitant-therapy group (33.5%) than in the triple therapy group (29%).
Conclusion: First-line moxifloxacin-based sequential and triple eradication therapy are comparable in *H. pylori* eradication rates with an acceptable safety profile. Sequential protocol showed better results, but statistical difference was not reached.

Abstract no.: P11.48

THIRD-LINE RESCUE THERAPY WITH MOXIFLOXACIN OR LEVOFLOXACIN-BASED TRIPLE REGIMEN FOR *HELICOBACTER PYLORI* INFECTION IN AREA WITH HIGH QUINOLONE-RESISTANCE

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Introduction: The recent increase in resistance of *H. pylori* against fluoroquinolone has become a significant limitation in effective eradication. The aim of this study was to evaluate the efficacy and tolerability of quinolone-based third-line rescue therapy for *H. pylori*.
Methods: From April 2003 to December 2013, a total 63 patients who experienced two consecutive eradication failures were included in this study. They received a 7-day standard triple regimen with proton pump inhibitor (PPI) (standard dose b.i.d.), amoxicillin (1000 mg b.i.d) plus either moxifloxacin (400 mg q.d.) (PAM group, n = 28) or levofloxacin (500 mg b.i.d.) (PAL group, n = 35) as a third-line rescue therapy for *H. pylori*. *H. pylori* eradication was evaluated by the ^{13}C-urea breath test, histology, or the rapid urease test. The eradication rate, drug compliance, and adverse event rates were compared between the two groups.
Results: The eradication rates by intention-to-treat analysis were 39.3% (11/28) and 57.7% (15/35) in the PAM group and the PAL group, respectively ($p = 0.802$). The eradication rates by per-protocol analysis were 45.8% (11/24) and 45.5% (15/33) in the PAM group and the PAL group, respectively ($p = 1.000$). Compliance was good in the both groups (PAM/PAL group: 87.5%/93.9%). The adverse event rates were reported in 45.8% (11/24) and 15.2% (5/33) in the PAM group and the PAL group, respectively ($p = 0.017$).
Conclusions: Efficacy of quinolone-based regimen has recently decreasing in Korea. Reconsiderations on fluoroquinolone-based rescue therapy for *H. pylori* is needed in the future.

Abstract no.: P11.49

NEUTROPHIL'S NADPH OXIDASE AS A THERAPEUTIC TARGET IN *H. PYLORI* INFECTIONS

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Background: During a *H. pylori* infection, massive amounts of neutrophils gather in the stomach mucosa. To eradicate the pathogen, activated neutrophils assemble NADPH oxidase (Nox) to convert oxygen into antimicrobial superoxide radicals. However, *H. pylori* can evade phagocytic killing by disrupting Nox targeting, resulting in extracellular reactive oxygen species (ROS) that continuously damage the gastric epithelium. Pharmacological modulation of ROS production may be an interesting approach to tackle *H. pylori*-induced gastritis. This study proposes electron paramagnetic resonance (EPR) to assess the effect of experimental compounds on ROS production by neutrophils.
Materials and Methods: Neutrophils from healthy volunteers were stimulated with phorbol 12-myristate 13-acetate (PMA) or opsonized zymosan (OPZ) to activate Nox. To monitor Nox assembly, Western blotting for phosphorylated p47phox was performed. The spin probe PPH trapped extracellular free radicals for EPR quantification. To identify the fraction of superoxide molecules, neutrophils were treated with superoxide dismutase (SOD). EPR was applied to evaluate the effect of test compound X on ROS production by neutrophils.
Results: PMA and OPZ stimulation of neutrophils led to Nox assembly. EPR allowed the quantification of ROS and identification of the superoxide fraction. Compound X decreased superoxide production by neutrophils.
Conclusions: EPR spectroscopy allows qualitative and quantitative assessment of the effect of compounds on ROS production by neutrophils. Compound X successfully inhibited the respiratory burst and is currently under investigation in vivo.

Abstract no.: P11.50

4-TIMES-DAILY DOSING OF ESOMEPRAZOLE ATTAINED POTENT ACID INHIBITION IRRESPECTIVE OF CYP2C19 GENOTYPES IN HEALTHY JAPANESE INDIVIDUALS

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Background: To attain higher eradication rates, potent acid inhibition (i.e. pH >6.0) by a PPI is required irrespective of CYP2C19 genotypes. Although esomeprazole (20 mg, bid) exert quite potent acid inhibition in CYP2C19 rapid metabolizers (RMs) compared to other PPIs, it does not reach the target value of the above-mentioned. We examined the efficacy of esomeprazole qid to set an optimum PPI regimen during eradication therapy.
Methods: In a randomized cross-over study, 30 healthy young Japanese volunteers (10 RMs, 10 intermediated metabolizers [IMs] and 10 poor metabolizers [PMs] of CYP2C19) received esomeprazole 20 mg bid or qid for 1 week. Intragastric pH monitoring was performed on Day-7.
Results: The median pH attained with esomeprazole 20 mg qid in all subjects was 6.8 (4.5–7.8), which was significantly higher than that of bid (5.5 [3.5–7.2], $p < 0.0001$). The median pHs attained with the bid and qid regimen were 5.3 (3.5–6.8) and 6.6 (4.5–7.5) in RMs, 5.5 (4.3–6.2) and 6.8 (5.9–7.7) in IMs, 6.2 (5.2–7.2) and 7.0 (5.0–7.8) in PMs, respectively. The median pHs with the qid were significantly higher than those with the bid in RMs ($p = 0.022$), IMs ($p = 0.005$) and PMs ($p = 0.047$). Although the median pHs with the bid differed significantly among different CYP2C19 genotypes ($p = 0.004$), those with the qid were similar ($p = 0.384$).
Conclusions: Four-times-daily dosing of esomeprazole 20 mg achieved potent acid inhibition, suggesting that HP eradication therapy based on esomeprazole 20 mg qid might have efficacy for Japanese patients failed by standard eradication therapy.

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This abstract has been withdrawn.

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CLINICAL CHARACTERSTICS AND OUTCOMES OF ANGIODYSPLASIA PRESENTED AS UPPER GASTROINTESTINAL BLEEDING

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Background: Angiodysplasia is considered as the differential diagnosis of upper gastrointestinal bleeding (UGIB), but the clinical features and outcomes associated with UGIB from angiodysplasia have not been characterized.
Aim: To analyze the clinical characteristics and outcomes of angiodysplasia presented as UGIB.
Methods: Between January 2003 and December 2012, a consecutive series of patients who had UGIB and admitted to St. Vincent's hospital, the Catholic University of Korea were retrospectively analyzed. A total of 35 patients with bleeding from angiodysplasia were enrolled in this study. We compared the UGIB group from angiodysplasia with asymptomatic control group (incidental findings of angiodysplasia during endoscopic examination in health screening center).
Results: When patients with UGIB from angiodysplasia were compared with asymptomatic control group, there were significant differences of age, hemoglobin level, hematocrit, blood urea nitrogen, sodium, albumin, fasting blood sugar (FBS), location (body/ fundus) and size of the lesion (≥1 cm) in univariate analysis. Also, the history of diabetes (FBS ≥126 mg/dL or HbA1c ≥6.5% or on medication) and medication history (anti-platelet agents, warfarin, NSAIDs, steroids) were different. In multivariate analysis, there were significant differences of the level of albumin, sodium, FBS, location and size of the lesion. The rate of clinical recurrence of UGIB from angiodysplasia was 14.2% (5/35).
Conclusions: When angiodysplasia was larger than or equal to 1 cm or located in gastric body/ fundus, it was associated with UGIB. In patients with angiodysplasia, strict control of blood sugar and good general condition might reduce the risk of bleeding.

Abstract no.: P11.53

THE RELATIONSHIP BETWEEN *HELICOBACTER PYLORI* INFECTION AND DE NOVO EROSIVE REFLUX ESOPHAGITIS

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Introduction: The previous studies have suggested a negative association between *Helicobacter pylori* eradication and the development of endoscopic erosive reflux disease (ERD) in Asian population. However, they included very few studies especially from Asian countries. We aimed to elucidate the association between *H. Pyroli* infection and ERD.
Method: This is a retrospective chart review of *H. pylori*-positive patients without endoscopic esophagitis who have visited for *H. pylori* eradication from January 1, 2013 to December 2013. They subsequently underwent gastroscopy after eradication. We analyzed the association and risk factors between *H. pylori* eradication failure (n = 30) and eradication successful group (n = 32).
Results: The median age of patients were 64 (52.71)/61 (51.71) years, respectively ($p = 0.60$). The median duration of follow-up were 25 (6.68)/25 (10.44) months ($p = 0.328$). By the end of follow-up period, de novo endoscopic esophagitis were more prevalent in the Successful group than in the Failed group (16.7% / 34.4%, $p = 0.15$) but the trend was not statistically significant. Univariate and multivariate analysis revealed no significant association between the incidence of ERD and age, gender, alcohol intake, smoking, weight change, or the presence of a hiatus hernia.
Conclusions: We observed a trend that the incidence of de novo endoscopic esophagitis was more common in *H. pylori* eradicated group than eradication failure group. This clinical characteristic may suggest differences in the geographic or ethnic background. A large cohort study to assess the potential relationship between *H. pylori* infection and ERD is needed.

Abstract no.: P11.54

COMPARING THE EFFICACY OF *HELICOBACTER PYLORI* ERADICATION IN VINNITSYA (UKRAINE) ON THE RESULTS OF THE RESPIRATORY UREASE TEST

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Modern gastroenterology should solve a big problems associated with resistance of *Helicobacter pylori* (HP) to antibiotics. Also the use of schemes of bismuth become topical in the first stage of antihelicobacter pharmacotherapy.
Objective: To compare the effectiveness of the eradication schemes of HP at 2007–2012. There were analyzed 274 results of a controlling urea breath test using 13C-urea (127 men and 147 women). The first group (146 patients) received: standard dose IPP b.i.d., clarithromycin 0.5 g b.i.d. and amoxicillin 1.0 g b.i.d. (IPP + K + A). The second group (48 patients) were prescribed triple therapy: standard-dose IPP b.i.d., clarithromycin 0.5 g b.i.d. and 0.5 g ornidazole b.i.d. (IPP + K + O). The third group (80 patients) received the quad therapy: IPP standard dose b.i.d., clarithromycin 0.5 g b.i.d., amoxicillin 1.0 g b.i.d. and bismuth subcitrate 0.24 b.i.d. (IPP + K + A + B). The duration of therapy was 7 days. Negative results of the urea breath test was diagnosed in 82.2% patients of the first group, 77.1% patients of the second group and 92.5% patients of the third group. Comparing the results of successful eradication of HP between the first (IPP + K + A) and the second group (IPP + K + O) we haven't found any significant differences ($p > 0.05$). While the level of successful eradication of the third group was significantly higher ($p < 0.01$).
Thus, quad therapy based on IPP + K + A and bismuth subcitrate is a highly eradication scheme in Vinnitsya.

Abstract no.: P11.55

EFFECT OF KOREAN RED GINSENG EXTRACT ON PPI-TRIPLE THERAPY FOR *HELICOBACTER PYLORI* ERADICATION

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Background and Aim: Triple therapy consisting of a proton pump inhibitor (PPI) and the two antibiotics of clarithromycin (CAM) and amoxicillin (AMPC)

has been used for the eradication of *Helicobacter pylori* as a first-line therapy. However, the eradication rate recently fell to around 70% because of an increase in CAM-resistant *H. pylori*. In order to find a new adjuvant agent for eradication therapy, we studied the effect of Korean Red Ginseng Extract® (KRGE) containing a large amount of saponin.

Methods: The effect of KRGE containing a large amount of saponin was studied in a CAM-resistant *H. pylori*-infected mice model. We also conducted a pilot study on KRGE supplementation with triple therapy in patients with *H. pylori* infection.

Results: A marked increase in the sensitivity of CAM-resistant *H. pylori* to the antibiotics induced by KRGE was expected due the action of saponin, a main component of KRGE. KRGE supplementation with triple therapy resulted in a far better eradication rate than triple therapy alone in the treatment of CAM-resistant *H. pylori*-infected mice. In patients with *H. pylori* infection, the eradication rate of KRGE plus triple therapy was 93.1% (27/29).

Conclusion: This study showed that triple therapy with KRGE improved the efficacy of first-line *H. pylori* eradication therapy.

Abstract no.: P11.56

S-ALLYL CYSTEINE TO ATTENUATE *HELICOBACTER PYLORI*-GASTRITIS AND GASTRIC CANCER VIA HISTIDINE DEACETYLASE INHIBITION

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S-allyl cysteine (SAC) synthesized from garlic efficiently prevented *Helicobacter pylori*-associated gastric carcinogenesis through rejuvenating chronic atrophic gastritis in addition to preventing cysteamine-induced duodenal ulcer, water immersion restraint stress-induced gastric ulcer, and NSAID-induced gastrouodenal damages. The rejuvenating action of SAC has rendered the significant changes of gastric microbiomes reflecting the effective changes of gastric microenvironment in accordant with amelioration of atrophy. SAC was pretreated 1 hours before *H. pylori* on RGM1 cells. MTT assay, DPPH assay, and DCF-DA spectroscopy were done to check anti-oxidative action of SAC. SAC had excellent efficacy by scavenging ROS on both DPPH assay and DCFDA study, whereas the expressions of SOD-1 and GPX (glutathione peroxidase) were significantly increased after SAC treatment. SAC significantly decreased inflammatory cytokine, IL-1β as well as the expression of pro-inflammatory enzymes, COX-2 and IL-8 against *H. pylori*. Centrally to these beneficiaries, SAC had significant HDAC inhibition effect through suppressing HDAC3 and activating Acetylated H3 and induced the expression of anti-apoptosis protein, Bcl-2 and Heat shock protein, HSP70 chaperone for gastric cytoprotecton. All of these mechanisms led to significant attenuation of *H. pylori*-chronic atrophic gastritis, resulting in the prevention of gastric cancer. Molecular targeted prevention should be applied to avoid from *H. pylori*-associated gastric carcinogenesis, about which HDAC inhibition of SAC might be central and prerequisite action.

Abstract no.: P11.57

CONCOMITANT TREATMENT AGAINST *H. PYLORI* INFECTION IN A GREEK POPULATION- A MULTIVARIATE ANALYSIS

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Introduction: High clarithromycin and metronidazole resistance rates in our country has set the quest for effective first-line treatments that align with the updated European guidelines.

Aim: Presentation of preliminary results of a perspective study of the concomitant treatment (CT) used for first-line *H. pylori* eradication, with an attempt to allocate possible factors that may relate with a successful eradication.

Method: 108 outpatients (Average Age: 52.9 years, M:39, F:69), diagnosed as H.P-positive, were interviewed using a preformed questionnaire, recording: sex, age, smoking, alcohol consumption, NSAID and long-term PPI intake, symptoms, anemia, personal history from upper GI and family history (FH) of gastric Ca. All received 10-day CT: PPIs × 2, Amoxicillin 1 g × 2, Clarithromycin 500 mg × 2 plus Tinidazole 500 mg × 2. 6–8 weeks after ending of treatment, all patients received UBT and compliance control. Results were analyzed per-protocol (PP analysis) and by univariate logistic regression analysis (z test).

Results:

Eradicate	♂/♀	Age 45≥/45<	Smoking −/+/ex	Alcohol −/+	NSAID −/+	Dyspepsia −/+	GOR −/+
+	36/62	71/27	39/31/28	85/13	85/13	34/64	46/52
−	3/7	8/2	3/1/6	8/2	8/2	3/7	5/5
Eradicate	Anemia −/+	Gastric ulcer −/+	Duodenal ulcer −/+	PPIs −/+	FH Ca −/+		
+	64/34	94/4	83/15	84/14	87/11		
−	7/3	8/2	10/0	7/3	9/1		

PP: 90.74% (90.74% eradicated *H. pylori*).

None of the parameters studied showed any statistically significant difference between patients that achieved eradication and those that did not.

Conclusion: So far, the concomitant treatment, used as first-line eradication regiment against *H. pylori*, appears effective enough for Greek H.P positive patients and in alignment with the European guidelines. None of the factors under study was related with the eradication result.

Abstract no.: P11.58

ANTIBIOTIC-METAL COMPLEXATION: AN APPROACH TO HELICOBACTER THERAPY

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Novel organometallic compounds have been prepared by complexing the fluoroquinolones, norfloxacin, ofloxacin, ciprofloxacin, sparfloxacin, lomefloxacin, pefloxacin and gatifloxacin, with bismuth, zinc, Iron, Copper and Manganese. The complexes were characterized by UV, IR, atomic absorption spectroscopy, elemental analysis, differential scanning calorimetry, thermogravimetric analysis and mass spectrometry. Their antibacterial potential against *Helicobacter pylori* and other microorganisms was investigated. These compounds were found to possess strong activity against *Helicobacter pylori* with a minimum inhibitory concentration of 0.5 mg L-l. They also exhibited moderate activity against *Escherichia coli,Staphylococcus aureus, Bacillus pumilus* and *Staphylococcus epidermidis.* These bismuth-fluoroquinolone complexes have the potential to be developed as drugs against *H. pylori* related ailments.

Abstract no.: P11.59

THE INFLUENCE OF VARIOUS *HELICOBACTER PYLORI* ERADICATION SCHEMES ON THE MICROORGANISMS OF THE COLON IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

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It was found that GERD patients have qualitative and quantitative changes in the microorganisms of the colon compared to healthy. Antimicrobials used for eradication of *Helicobacter pylori* (*H. pylori*) may affect the condition of the colon microorganisms and consequently lead to a risk of the onset of symptoms of GERD.

Objective: To study the effect of H.P. eradication schemes on the microorganisms of the colon in patients with GERD. The study included 30 patients with GERD who was infected with H.P.

The first group took lansoprazole 0.03 g b.i.d., clarithromycin 0.5 g b.i.d. and amoxicillin 1.0 g b.i.d. (L+R+A). The second group took lansoprazole 0.03 g b.i.d., tetracycline 0.5 g b.i.d., metronidazole 0.5 g b.i.d., 0.12 g of bismuth subcitrate b.i.d. (L+T+ M+B). In the group L+R+A found that after eradication E. coli didn't differ significantly ($p > 0.05$) compared to before treatment (8.6 lg7 ± 6.2 lg7 CFU/g vs 1.02 lg8 ± 6.7 lg7 CFU/g). It does not found significant ($p > 0.05$) differences between the amount of lacto- and bifidum bacteria before and after the treatment.

Under the influence of the scheme L+R+A observed non-significant increase ($p > 0.05$) weak-enzyme E. coli and hemolyzing E.coli compared with those before treatment microorganisms.

In analyzing the quantitative results of bacteriological examinations in the group L+T+ M+B it was found that after treatment had significant ($p < 0.05$) reduction of lacto- and bifida bacteria and significant increase ($p < 0.05$) in cocci-forming microflora of the colon compared to before treatment.

Scheme eradication of H.P. L+T+M+B results in a reduction of saprophytic microflora of colon.

Abstract no.: P11.60

ANTI *HELICOBACTER PYLORI* REGIMENS SIDE EFFECTS: FREQNENCY AND IMPACT ON COMPLIANCE TREATMENT

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Aim: To evaluate the frequency of side effects in patients treated by anti *Helicobacter pylori* (Hp) regimens and their impact on treatment compliance.

Patients and Methods: From 2002 to 2011, we collected, in a prospective, unicentric and randomized study, data of 382 Hp positive patients treated by OAM 10, OAM7,OAC7, OMC7 and Rbct regimens (mean age: 38.3, males: 121, DNU: 295, DU: 87). During the treatment, patients have possibility to contact investigators by telephone or to come for clinical check up in case of new event. At the end of the protocol, side effects have been looked up by clinical questionnaire. Therapeutic compliance was assessed by recovering of not consumed tablets. It was defined as very good when patients consumed 100% of tablets.

Results: Side effects were noted in 48% of cases. Their intensity was always mild to moderate. Digestive disorders were the most frequently noted sides effects (85.9%). Diarrhea, abdominal pain, ageusia and vomiting were observed in respectively 12.5%, 9.3% 7% 0.2% of cases. Clarithromycine regimens were more frequently responsible of abdominal pain (OAC7:23.2%, OMC7:14.7%, OAM10:6.6%,OAM7:5.3%, Rbct:3.7%).Global observance was very good in 97.4% of patients. Side effects were rarely the cause of a treatment interruption (3.5% of cases).

Conclusion: Side effects induced by anti Hp regimens were frequent. They were mostly gastrointestinal effects, always minimal to moderate and rarely the cause of treatment interruption.

P12 NSAIDs, COXIBs, ASA and *H. pylori* Infection

Abstract no.: P12.01

CHANGING TRENDS IN THE AETIOLOGY OF PEPTIC ULCER DISEASE IN A TERTIARY HOSPITAL OF GERMANY

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Background: A decline in prevalence of peptic ulcer disease (PUD) due to the decreasing prevalence of *Helicobacter pylori* (*H. pylori*)-infection has been reported.
Aim: To determine the prevalence of endoscopic PUD and its aetiology in a tertiary hospital of Germany.
Methods: Patients with PUD diagnosed by endoscopy from 05/2001 to 12/2002 and from 01/2006 to 12/2010 were identified in the digital archive of the Otto-von-Guericke University Hospital. Demographics and intake of aspirin/non-steroidal anti-inflammatory drugs (NSAIDs) were documented. Subjects with positive results for at least one assay among histology, 13C-urease breath test, rapid urease test or serology were classified as *H. pylori*-positive. Collected data were compared between the two groups.
Results: 1007 Patients with PUD were identified, 172 (male 56.4%, mean age 63.2 years) in the period 2001/2002 and 835 (male 60.1%, mean age 65.6 years) in the period 2006–2010. The rate of endoscopic PUD increased from roughly 100 to 165 per year over the study period. The prevalence of *H. pylori* infection decreased from 52.8% to 38.4% ($p = 0.004$) whereas the prevalence of aspirin/NSAID intake increased from 37.5% to 47% ($p = 0.03$) among patients with PUD. In both groups roughly 15% of PUD patients had both risk factors. The proportion of idiopathic PUD was 27% and 30% in the period 2001/2002 and 2006–2010, respectively.
Conclusions: The rate of endoscopic PUD in our institution increased over the study period. Aetiology of PUD changed substantially with a decrease of *H. pylori*-positive PUD and an increase of PUD associated with aspirin/NSAID intake.

Abstract no.: P12.02

TIME-RELATED VARIATION IN GASTROINTESTINAL LESIONS AMONG NON-STEROIDAL ANTI-INFLAMMATORY AND ASPIRIN USERS WITH OR WITHOUT *H. PYLORI* INFECTION

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Background: *H. pylori* infection has been shown to approximately double the risk of non-steroidal anti-inflammatory drug (NSAIDs) including aspirin of peptic ulcer disease complications.
Aim: To analyze the prevalence of gastrointestinal (GI) lesions (ulcer and/or erosions) in relation to *H. pylori* status, NSAIDs and ASA use in a cohort of patients that underwent upper endoscopy for dyspeptic symptoms.
Methods: Patient records scheduled for upper endoscopy were acquired and retrospectively reviewed. Patients with gastric histology available for *H. pylori* identification and 13C-UBT or rapid urease test were included from 1995 until 2011 were included.
Results: A total of 11 360 records were analyzed. Gastric and duodenal ulcer and/or erosions were significantly more common in patients positive for *H. pylori* (eg, in 1995: 14.7% vs 9.4%) whereas in 2011 the prevalence had decreased the difference remained (eg, 1.8% vs 0.5% for infected vs uninfected, respectively). GI lesions were significantly more common in NSAID takers irrespective of *H. pylori* status and this difference remained over time (i.e., lesions were found in 21.1% of uninfected NSAID users in 1995 and 4.2% in 2011 vs 47% and 7.7% in *H. pylori* infected individuals in 2011.
Conclusions: Both *H. pylori* infection and NSAID use independently and significantly increase the risk for peptic ulcer and/or erosions. Peptic-ulcer disease is rare in *H. pylori* negative non-NSAID-ASA user Sardinians undergoing endoscopy for evaluation of dyspepsia. The rapid decline of gastrointestinal lesions associated with *H. pylori* infection and with NSAID use may relate to the increased use of proton pump inhibitors.

P13 Drug Resistance

Abstract no.: P13.01

ANTIBIOTIC RESISTANT PATTERN OF *HELICOBACTER PYLORI* INFECTION IN THE SOUTH AND SOUTHEAST ASIAN COUNTRIES

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Objective: Aim of this study was to survey antibiotic resistant of *H. pylori* infection in South and Southeast Asian countries including Thailand, Laos, Bhutan and Myanmar and to determine factors associated with antibiotic resistance.

Methods: Total of 4998 strains were enrolled in this study (3964 Thailand, 329 Laos, 372 Bhutan and 333 Myanmar). EGD were performed in dyspeptic patients during May 2004 and April 2013. Three antral biopsies were obtained for culture, E-test or HelicoDR to detect mutations for clarithromycin and fluoroquinolone resistances.

Results: 1846 patients (36.9%) were infected with *H. pylori* (35.1% in Thailand, 36.2% in Laos, 73.4% in Bhutan and 31.2% in Myanmar). Prevalence of antibiotic-resistant *H. pylori* was summarized in Table 1.

Table 1 Antibiotic resistant *H. pylori* in each country

Antibiotics (n = 682)	Thailand (n = 400)	Laos (n = 119)	Bhutan (n = 111)	Myanmar (n = 52)
Amoxicillin (MIC 0.25 μg/mL)	5.2%	–	0%	0%
Clarithromycin (MIC 1 μg/mL)	3.7%	12.6%	0%	0%
Metronidazole (MIC 8 μg/mL)	36%	–	82.9%	36.5%
Tetracycline (MIC 1 μg/mL)	1.7%	–	0%	0%
Ciprofloxacin (MIC 1 μg/mL)	7.7%	13.4%	2.7%	5.8%
Levofloxacin (MIC 1 μg/mL)	7.2%	13.4%	2.7%	5.8%

Some factors were associated with antibiotic resistance eg. In Thailand, age> 40 years had higher prevalence of clarithromycin resistance than age<40 years (4.7% vs 0%; p-value = 0.04). In Laos, BMI ≥25 were significantly higher prevalence of clarithromycin resistance than BMI <25 (20.5% vs 8%, p-value = 0.048).

Conclusion: *H. pylori* infection remains major health problem in Asian countries. Metronidazole resistance was high and remains the most common antibiotic resistace in this area. Clarithromycin and fluoroquinolone are still useful. Knowing pattern of antibiotics used in *H. pylori* eradication will permit optimal choices for the best outcome in each geographical location.

Abstract no.: P13.02

ANTIMICROBIAL RESISTANCE IN *HELICOBACTER PYLORI* AND ITS RELATIONSHIP WITH CONSUMPTION OF ANTIBIOTICS

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The aim of this study was to determine the antimicrobial resistance in *H. pylori* and the consumption of 3 antibiotics in the same health area.

245 *H. pylori* strains from 2009 to 2013 were studied. Biopsies obtained from endoscopy were cultured in Pylori Agar and antimicrobial susceptibility performed by E-test. Consumption of clarithromycin (CLR), levofloxacin (LVX) and metronidazole (MTZ) in 2010 and 2013 was studied as defined daily doses (DDD) and expresed as DDD per 1000 inhabitants and day (DID). Statistic analysis was performed by chi-square and Pearson correlation.

Global resistance rate was 53.8% for CLR, 6.9% for LVX and 34.9% for MTZ. Consumption as DID are shown in the table:

DID in 2010 and 2013

	2010	2013	TOTAL
CLR	0.125	0.09	0.216
LVX	0.102	0.09	0.192
MTZ	0.01	0.011	0.021

Consumption of the 3 antibiotics acording the prescript department

	Gastroenterology Department	Pneumology	Others
CLR	74.1%	1.6%	24.3%
LVX	8.3%	26.4%	65.3%
MTZ	67.2%	2.9%	29.9%

Gastroenterology Department was the higher prescript for CLR and MTZ and Pneumology the higher prescript for LVX. CLR consumption decreased a 28.5%, LVX decreased a 12.6% and MTZ increased a 8.9% from 2010 to 2013. A significant association among decreasing consumption and resistance was found for LVX. However, this association was not observed with CLR nor MTZ.

In this study a high resistance rate to CLR was observed and a decreasing in its consumption does not correlated with a resistance decrease, at least in the period studied.

Abstract no.: P13.03

RANDOMIZED CLINICAL TRIAL: COMPARISON OF CONCOMITANT THERAPY WITH HYBRID THERAPY FOR *HELICOBACTER PYLORI* ERADICATION

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Background: In the era of increasing resistance of *Helicobacter pylori* against antibiotics, non-bismuth-containing regimens have been validated for the optimal treatment.

Aims and Methods: We aimed to identify the superb treatment option comparing concomitant and hybrid regimen as a first-line treatment for *H. pylori* infection. A total of 485 naïve *H. pylori*-infected patients from six hospitals in Korea were randomly assigned to concomitant and hybrid therapy groups. The concomitant regimen consisted of 20 mg of esomeprazole, 1 g of amoxicillin, 500 mg of clarithromycin, and 500 mg of metronidazole, twice daily for 10 days. The hybrid regimen consisted of a 5-day dual therapy (20 mg of esomeprazole, and 1 g of amoxicillin, twice daily) followed by a 5-day quadruple therapy (20 mg of esomeprazole, 1 g of amoxicillin, 500 mg of clarithromycin, and 500 mg of metronidazole, twice daily).

Results: Concomitant and hybrid eradication rates were 78.6% (187/238) vs 78.8% (190/241) by intention-to-treat (p = 0.943) and 90.3% (176/196) versus 89.6% (181/202) by per-protocol (p = 0.829), respectively. The incidence of adverse events was similar between the two groups.

Conclusions: Concomitant and hybrid therapy were proven to be equally efficient regimens as the first line treatment option for *H. pylori* infection.

Abstract no.: P13.04

CHANGES IN THE ERADICATION RATES OF FIRST AND SECOND-LINE THERAPY FOR *HELICOBACTER PYLORI* AT THE CLINIC OF A COMPANY FOR THE PAST 17 YEARS IN JAPAN

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Background: Standard first-line eradication therapy for *Helicobacter pylori* (*Hp*) infection is a proton pump inhibitor (PPI), amoxillin (AMPC), and clarithromy-

cin (CAM) for 7-day in Japan. However, the eradication rate decreases as the CAM resistance ratio rises. We studied primary and second eradication results for patients with *Hp* infection in one Japanese company for the past 17 years and determined eradication rate changes, retrospectively.

Methods: We assessed 544 subjects (23–61 years, 528 men) receiving Japanese first- and second-line eradication therapies (1996-2013) in the company clinic among approximately 3,500 employees and examined *Hp* eradication rates. We conducted upper GI endoscopy. Infection was confirmed by serological testing or rapid urease test, and eradication success was primarily confirmed using urea breath testing.

Results: Eradication was successful in 445 cases. Based on intention-to-treat (ITT)/per-protocol (PP) the first eradication rates were 81.8%/84.1%. In 57 cases before 2001 ITT/PP was 96.5%/96.5%. For 2002-5 (88 cases) ITT/PP was 87.5%/88.5%. For 2006-9 (150 cases) ITT/PP was 80.0%/82.2%. For 2010–2013 years (215), ITT/PP was 77.7%/81.5%. A second-line eradication with PPI, AMPC and metronidazole was required for 76 cases (74 men). Treatment was successful in 67 cases, with ITT/PP being 88.2%/91.8%. During the 2002-7 period there were 13 cases, and ITT/PP was 92.3%/100%. During the 2008-9 period (18) ITT/PP was 88.9%/88.9%. During the 2010-11 period we had 2 cases and ITT/PP was 86.2%/89.3%. During a 12–13 year period we had 16 cases and ITT/PP was 87.5%/93.3%.

Conclusions: Although the first-line eradication rate decreased, second eradication rates have remained stable since 2006.

Abstract no.: P13.05

ESTABLISHMENT OF HIGH RESOLUTION MELT CURVE ASSAY FOR THE DETECTION OF POINT MUTATIONS ASSOCIATED WITH CLARITHROMYCIN RESISTANCE IN *HELICOBACTER PYLORI*

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Clarithromycin is used in the first line treatment of *Helicobacter pylori* (HP) infection and therefore, the prevalence of HP resistance to clarithromycin is increasing continuously.

Clarithromycin resistance, the major cause of HP treatment failure, is attributed to three point mutations (PM): A2142C, A2142G and A2143G within the peptidyl-transferase region of the 23 S rRNA gene. Our aim was to develop a fast and accurate method for the detection of the three mutations mentioned previously, from HP isolates.

A total of 85 HP isolates, previously obtained from patients with general gastric discomfort, were analyzed using a high resolution melt (HRM) curve analysis. The isolates were compared to 4 reference plasmids that incorporate the three mutations and the wild type (WT) sequences. There was a perfect correlation between the HRM results and the 85 positive isolates - all were positive using the HRM analysis.

Of the 85 isolates, 18 had a WT sequence (21.2%), and 67 (78.8%) contained a 23 S rRNA PM. Of the 67 isolates that include 23 S rRNA PM, 18 had an A2142G PM sequence (26.8%), 22 had an A2142C PM sequence (32.8%) and 27 had an A2143G PM sequence (40.4%).

Our developed HRM assay has a perfect correspondence in its accuracy to other detection methods, including HP isolation. It serves as an option for detecting Clarithromycin resistance prior to administration of HP eradication therapy.

Abstract no.: P13.06

DOES TAILORED THERAPY BASED ON ANTIMICROBIAL SUSCEPTIBILITY TESTING OVERCOME THE INCREASING FAILURE OF STANDARD EMPIRICAL THERAPY FOR *HELICOBACTER PYLORI* INFECTION?

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Due to increased resistance to empirical antibiotics, eradication rates have fallen considerably short of the 80% (intention to treat rates) that are considered minimal acceptable levels as recommended in Maastricht guidelines. Study aimed to compare efficacy of standard empirical therapy with tailored therapy based on antimicrobial susceptibility. In this study treatment naïve *H. pylori* patients as assessed by CLO-test were invited to participate. Antral biopsy was processed for antimicrobial susceptibility employing both standard culture, E-testing & genotyping for resistance. Patients were randomised to receive either empirical or tailored treatment which included standard triple therapy or if resistance was detected triple therapy with Amoxicillin, Levofloxacin & PPI or quadruple therapy & follow up UBT was performed. To date 247 patients had CLO tests assessed & 52 (21%) were *H. pylori* positive. Infected patients tend to be younger men (mean age 47 vs 53 years), $p < 0.05$ & 56% versus 46% were male. In all 47 (90%) patients have been randomised & 40(85%) have completed study. Of 40, 15 (37.5%) & 25 (62.5%) received tailored & empirical therapy respectively. In tailored arm 6 (40%) received quadruple & 4 (27%) Levofloxacin & 5 (33%) standard triple therapy. Eradication rates were higher in tailored group i.e. 87% (13/15): 68% (17/25). 42% of strains were clarithromycin resistant & 7 of 8 (88%) patients who failed empirical therapy had resistant strains ($p < 0.001$). Study showed resistance levels to clarithromycin are high at 42%. Targeted therapy can enhance eradication & larger numbers required before a new first line treatment can be recommended.

Abstract no.: P13.07

EFFICACY OF SEQUENTIAL THERAPY IN *HELICOBACTER PYLORI* NAÏVE PATIENTS WITH HIGH CLARITHROMYCIN RESISTANCE RATES

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Background: Sequential therapy achieves remarkable results also in patients harbouring resistant strains.

Objective: To assess the efficacy of Sequential therapy in eradicating naïve *Helicobacter pylori* patients with multi-resistant strains.

Methods: Between 2010 and 2014, consecutive patients undergoing gastroscopy were evaluated. ^{13}C-UBT was performed and 2 biopsies from the antrum, angulus, and corpus were obtained to perform histology. Further biopsies from antrum were taken to perform RUT and to carry out culture and antimicrobial sensitivity by Epsilometer test. According to EUCAST 2012 the following MIC breakpoints were used: > 0.5, > 8 and 1 μg/mL for clarithromycin, metronidazole and levofloxacin, respectively. Patients were considered infected if culture alone or histology and RUT were positive. All received standard Sequential therapy. Four to six weeks after the end of the treatment, eradication was assessed by ^{13}C-UBT.

Results: Up to date, 932 naïve consecutive *Helicobacter pylori* infected patients were enrolled. Follow up are now available in 911 out of 932; eradication rate was achieved in 867 out of 911 (95.2%; 95% CI: 93.8–97). Eradication rates according to antibiotic resistance pattern were provided in the Table.

Conclusions: Sequential therapy is able to overcome the problem of multi-resistant strains in a large proportion of patients. Sequential therapy may be the optimal treatment for patients suspected of having multi-drug resistant strains especially if clarithromycin is involved.

Resistance	Cases	Follow-up	Eradication (%)
Cla	266	259	90.7
Metro	296	288	93.0
Levo	210	206	92.8
Cla + Metro	164	160	86.6
Cla + Levo	116	112	88.8
Metro + Levo	136	133	92.6
Cla + Metro + Levo	92	89	89.1

Abstract no.: P13.08

IN VITRO ACTIVITY OF ARTEMISONE AGAINST DIFFERENT STRAINS OF *HELICOBACTER PYLORI*

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Artemisinin is a sesquiterpene lactone endoperoxide extracted from *Artemisia annua*. In addition to their antimalarial properties, artemisinin and its derivatives possess immunomodulatory and antitumor properties. It has been reported that artemisinin and derivatives are also active against *Helicobacter pylori*. The aim of this study was to evaluate the antibacterial activity of artemisone, a new derivative against both susceptible and resistant strains of *Helicobacter pylori* isolated from human subjects in Lombardia, Italy. Artemisone is a second-generation artemisinin that has shown improved pharmacokinetic properties including longer half-life and lower toxicity. The compound was tested against 25 clinical isolates and one reference strain of *H. pylori* using the broth microdilution methodology. In order to verify the rate and extent of killing of *H. pylori* by artemisone, kinetic of bactericidal action was also assessed against the reference *H. pylori* strain ATCC 43504. The growth inhibitory concentrations of artemisone against the clinical isolates were similar to bactericidal action, with values ranging from 0.25 to 0.5 μg/mL. Independent of their susceptibility to metronidazole or chlaritromycin, 90% of the clinical isolates displayed growth inhibition by artemisone at 0.5 μg/mL. A decrease of 4-$\log_{10}$ in cell count was observed after 48 hours at 0.5 μg/mL. Thus, artemisone displays promising antibacterial properties against *H. pylori*. Therefore, use of artemisone in combination with antibiotics represents a potentially novel strategy for the treatment of infection, especially in cases of multidrug resistant *H. pylori*.

Abstract no.: P13.09

WHICH TEST TO USE FOR DETERMINATION OF CLARITHROMYCIN AND LEVOFLOXACIN SUSCEPTIBILITY IN *HELICOBACTER PYLORI* INFECTION?

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Aim: To evaluate the effectiveness of GenoType HelicoDR(GTHDR) and Real-time PCR(RT-PCR) for antimicrobial susceptibility; and also to confirm determined mutations leading to clarithromycin and levofloxacin resistance by sequencing.

Methods: Antrum and corpus gastric biopsies and stool specimens of 58 patients were included and stool specimens of three patients could not be obtained.RT-PCR and GTHDR were used for both biopsy and stool specimens.DNA of biopsies and stool specimens were extracted (QIAGEN). E-test was also performed to determine clarithromycin and levofloxacin susceptibility in biopsy specimens. Biopsy DNA specimens with different results obtained by above methods were sent for sequencing to determine and confirm the point mutations in *rrl* and *gyrA* genes.

Results: Concordance between GTHDR and RT-PCR was 81% and 64.6% for determination clarithromycin wild-type, resistant and mixed-strains in biopsies and stool specimens, respectively.In addition, correlation between biopsy and stool specimens were 61.1% and 71.4% for clarithromycin by GTHDR and RT-PCR, respectively.RT-PCR results had a better correlation than GTHDR with sequencing results. Most specimens were detected mixed genotype by GTHDR, while they were either wild-type or resistant by sequencing. Specimens with "no band mutation" at codon87 were determined N87I mutation by sequencing for levofloxacin.RT-PCR and GTHDR correlation with E-test were 73.0% and 63.3% to determine clarithromycin susceptibility in biopsy specimens, respectively.Correlation between GTHDR and E-test for levofloxacin was 67.3%.

Conclusion: The highest correlation was obtained between two molecular methods for clarithromycin susceptibility in biopsies.Although RT-PCR more correlated with E-test, GTHDR could be preferred because of its ability to determine clarithromycin and levofloxacin susceptibility simultaneously and also to detect mixed genotypes.

Abstract no.: P13.10

HIGH RATE OF CLARITHROMYCIN RESISTANCE IN *HELICOBACTER PYLORI* CLINICAL ISOLATES OBTAINED FROM CHILDREN IN GREECE: A RETROSPECTIVE STUDY, 2000–2013

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Helicobacter pylori (Hp) resistance to antibiotics is increasing worldwide, compromising the success of empirical anti-Hp standard regimens. Our aim was to evaluate the primary Hp resistance from children to conventional antibiotics during a 14-year period in Greece. Furthermore, we detected the gene mutations associated with clarithromycin and levofloxacin resistance.

The study enrolled 222 Hp clinical isolates from children (age 10.70 ± 3.16 years). For comparison purposes, the 2000–2013 timeframe was divided in three periods; period 2000–2005 (77 Hp isolates), period 2006–2009 (88 Hp isolates) and period 2010–2013 (65 Hp isolates). Hp antibiotic susceptibility was assessed by E-test, adopting the EUCAST MIC breakpoints. The presence of genetic mutations was determined by Real-Time PCR in clarithromycin-resistant and by sequencing analysis of the Hp gyrase A gene in Levofloxacin-resistant strains.

No resistance to tetracycline was detected. Resistance to amoxicillin was observed only in period 2000–2005 (3.9% [3/77]). An increase in clarithromycin-resistance and levofloxacin-resistance was observed in our study population, with prevalence rates, ranging from 26% to 47.7% and 2.5% to 6.2%, respectively. In contrast, metronidazole-resistance showed a decrease through the study period (from 35% to 21.5%). The predominant mutations correlated with clarithromycin-resistance were A2143G and A2142G in the 23S rRNA gene, and the Asn87Lys mutation in the gyrA gene for levofloxacin-resistant strains.

The high prevalence of Hp clarithromycin-resistance and the emergence of levofloxacin-resistance in children patients highlight the need for adopting an appropriate first line therapy on the basis of antimicrobial susceptibility testing, in order to avoid treatment failure and the development of secondary resistance.

Abstract no.: P13.11

TWO-YEAR MULTICENTER SURVEILLANCE OF *HELICOBACTER PYLORI* ANTIBIOTIC RESISTANCE FROM ADULT PATIENTS IN GREECE

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The increasing worldwide prevalence of *Helicobacter pylori* (Hp) antibiotic resistance is a major cause of treatment failure, with variations observed within and between countries. Our aim was to evaluate the primary resistance of Hp isolates from adult patients, from different regions of Greece, to conventional antibiotics and to detect the gene mutations associated with clarithromycin (CLA) and levofloxacin (LEV) resistance.

A total of 196 Hp isolates from adult patients (age 52.04 ± 14.93) were collected throughout the country over a 2-year period (2012–2014). Hp antibiotic susceptibility was assessed by E-test adopting the EUCAST MIC breakpoints. The presence of point mutations was analyzed by Real-Time PCR in CLA-resistant and by sequencing analysis of the Hp gyrase A gene in LEV-resistant strains.

No resistance to amoxicillin or tetracycline was detected. Overall, primary resistance levels to metronidazole (MET), CLA and LEV were determined at 34.7% (68/196), 25.5% (50/196) and 9.2% (18/196), respectively. Multi-drug resistance was observed for MET-CLA (17/196, 8.7%), for MET-LEV (5/196, 2.6%) and for MET-CLA-LEV (3/196, 1.5%). No statistically significant differences in

antibiotic resistance were found between Hp isolates from different regions of the country ($p > 0.05$). The predominant mutations correlated with CLA-resistance were A2143G and A2142G in 23S rRNA gene, and the Asn87Lys mutation in gyrA gene for LEV-resistant strains.
The high rates of primary antibiotic resistance, particularly to CLA, have been associated with the high antibiotic consumption observed in our country. This consideration highlights the importance of antibiotic susceptibility testing prior to the implementation of treatment strategies using CLA in our country.

Abstract no.: P13.12

MOLECULAR CHARACTERIZATION OF ANTIBIOTIC RESISTANCE IN ENTEROHEPATIC *HELICOBACTER* SPECIES

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Enterohepatic *Helicobacter* species (EHS) naturally colonize animals, and have been increasingly reported to causes colitis, gastroenteritis, bacteremia and cellulitis in humans. Numerous antibiotics have been prescribed for *H. pylori* eradiation; however, multiple strains of *H. pylori* have become multi-resistant. It has been reported that mutations in *H. pylori* 23S rRNA, 16S rRNA and gyrA genes are responsible for the resistance to clarithromycin, ciprofloxacin, and tetracycline. To ascertain if EHS antibiotic resistances are related to similar gene mutations, we investigated by E-test the antibiotic susceptibility profiles of 41 helicobacter strains isolated from animals and humans representing 24 different *Helicobacter* spp. (6 isolated from humans and 18 from animals). Ten of 41 strains (24%) were resistant to clarithromycin, and 80% of those resistant strains demonstrated an A2142G mutation in the 23S rRNA gene. Of the 32% of the strains resistant to ciprofloxacin, 92% contained mutations in the quinolone resistance-determining region (QRDR) of the gyrA genes (codons 87, 89 or 91). In addition, 12 of 41 (29%) of the EHS strains were resistant to tetracycline, with 58% demonstrating the AGA926 to 928→ TTC mutation in the 16S rRNA gene. EHS antibiotic resistance profiles varied by *Helicobacter* spp. and the host from which the EHS was isolated. Antibiotic resistance in EHS may be due, in part, to mutations in the 23S rRNA gene, 16S rRNA gene and/or the gyrA genes, comparable to those documented in *H. pylori*.

Abstract no.: P13.13

MUTUAL EFFECTS OF ANTIMICROBIAL COMBINATION AGAINST CLINICAL ISOLATES OF RESISTANT *HELICOBACTER PYLORI* IN VITRO

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Objective: To illuminate the effects of 15 groups of combinations that combined with each other by 6 kinds of antibiotics (A-Amoxicillin, C-Clarithromycin, M-Metronidazole, L-Levofloxacin, T-Tetracycline, F-Furazolidone) against antibiotic-resistant *H. pylori* in vitro.
Methods: The research was conducted by agar dilution method and checkerboard method to measure the minimal inhibitory concentrations of single and combined antibiotics against 33 strains of resistant H.pylori, then the fractional inhibitory concentration index (FICI) was calculated to evaluate effects. When FICI ≤0.5 was defined as synergism, 0.5 < FICI ≤ s1 as accumulation, 1 < FICI ≤ 2 as independence and FICI > 2 as antagonism.
Results: The FICI in 15 groups were respectively [Form: Drugα+ Drugβ= FICI (NO. of strains)]: (i) A+C = 0.5 (7), 0.75–1 (23), 1.25–2 (3) (ii) A+M = 0.5 (28), 0.75–1 (5) (iii) A+L = 0.5 (31), 0.75–1 (2) (iv) A+F = 0.5 (3), 0.75–1 (19), 1.25–2 (11) (v) A+T = 0.5 (3), 0.75–1 (8), 1.25–2 (12) (vi) C+M = 0.5 (9), 0.75–1 (24) (vii) C+L = 0.5(3), 0.75–1 (6), 1.25–2 (18), >2 (6) (viii) C+F = 0.75–1 (26), 1.25–2 (7) (ix) C+T = 0.75–1 (29), 1.25–2 (4) (x) M+L = 0.5 (13), 0.75–1 (14), 1.25–2 (6) (xi) M+F = 1.25–2 (33) (xii) M+T = 0.5 (7), 0.75–1 (17), 1.25–2 (9) (xiii) L+F = 1.25–2 (17), >2 (16) (xiv) L+T = 0.5 (18), 0.75–1 (15) (xv) F+T = 0.5 (13), 0.75–1 (20).
Conclusion:

1. In vitro, combination effects, such as A+M, A+L and L+T, were mainly synergistic, while A+C, A+F, C+M, C+F, C+T, M+L, M+T and F+T were additive. A+T, C+L, M+F and L+F primarily showed indifferent. Antagonistic action were showed in C+L (18.2%) and L+F (48.5%).
2. The same combinations showed various effects. Synergism and accumulation increased the sensitivity of strains to drug. It is noteworthy for physician to notice the importance of rational and efficient antimicrobial combination as antagonism also existed in combinations.

Abstract no.: P13.14

USING A NOVEL DEVELOPED HIGH RESOLUTION MELT CURVE ASSAY FOR THE ANALYSIS OF THE PREDOMINANCE OF *HELICOBACTER PYLORI* CLARITHROMYCIN RESISTANCE

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Helicobacter pylori (HP) is the most common pathogen found in humans. Its resistance to clarithromycin is increasing continuously and it is one of the main reasons for eradication failure. The resistance is attributed to three point mutations (PM): A2142G, A2142C and A2143G within the peptidyl-transferase encoding region of the 23S rRNA gene.
We aimed to analyze the predominance of HP clarithromycin resistance by using our novel high resolution melt (HRM) curve assay. A total of 32 HP stool samples were collected from patients with general gastric discomfort who also performed $^{13}CO_2$ breath tests (BTs). HP DNA was extracted from the stool and was analyzed by HRM. The results were compared to the BTs. The HRM positive results were further analyzed by comparing them to 4 reference plasmids incorporating the three mutations and the WT sequences.
The HRM results presented 25 positive and 7 negative samples - demonstrating a 53% clarithromycin resistance. When compared to the 21positive and 11 negative BT, the HRM had a sensitivity of 100% and specificity of 64%.
Of the 25 positive HRM samples, 6 (24%) had a WT sequence, 6 (24%) had an A2142G PM, 7 (28%) had an A2142C PM, 4 (16%) had an A2143G PM and 2 (8%) were heterozygote (multiple peaks).
Our study is consistent with other reports suggesting an increasing HP clarithromycin resistance worldwide. Further investigation is required in order to determine its prevalence in Israel. Moreover, our HRM assay may be used for screening prior to administration of clarithromycin eradication therapy.

Abstract no.: P13.15

ERADICATION OF *HELICOBACTER PYLORI* INFECTION WITH OPTIMIZED AND CONCOMITANT STARTEGIES IN A POPULATION WITH HIGH CLARITHROMYCIN RESISTANCE

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Objective: To determine de eradication rate achieved of *Helicobacter pylori* infection in a high-resistant clarithromycin population by applying 14-day classical triple therapy (OPT14), concomitant therapy during 10 and 14 days (CONCO10; CONCO14). To determine the rate of adverse effects present with these regimens.
Method: Retrospective analysis of naïve patients with *Helicobacter pylori* infection ttreated with OPT14 (amoxicillin 1 g/12 hours, clarithromycin 500 mg/12 hours, esomeprazo l40 mg/12 hours), CONCO10 AND CONCO14 (clarithromycin500 mg/12 hours, metronidazole 500 mg/12 hours, amoxicillin 1 g/12 hours, esomeprazo l40 mg/12 hours). Eradication was tested using the Urea breath test 8 weeks after therapy. Qualitative and quantitative variables were considered for de analysis, including gender, age, diagnosis, treatment regimen, compliance, and adverse effects.
Results: 87 patients (64.4%women, 35.6%men) with a mean age of 51.39 (± 16.09) were initially included (23%smokers, 8%non-investigated dyspepsia, 65.5%functional dyspepsia, 21.8%peptic ulcer, 4.6%other diagnosis). 25.3% received OPT14, 31% CONCO10, and 47.3% CONCO14. Eradication was achieved in 87.2% (CI 95%:79.56–94.84%) (OPT14 86.4%; CONCO10 88.5%; CONCO14 86.4%; p = ns). Mild adverse effects were observed in 25.3%, described the most with CONCO10 (48% of CONCO10). Adverse effects included abdominal pain (total 8%; 14.8% of CONCO 10. p = ns), metallic taste (total: 6.9%; 18.5% of CONCO10. $p = 0.015$), and diarrhea (total 5.7%; 14.8% of CONCO10), which did not condition treatment interruption.
Conclusions: The eradication achieved in our high clarithromycin-resistant population suggests that first-line treatment options including optimized 14 day

triple therapy and concomitant regimens improve our eradication rates and should be the first option in treating naïve patients. Although ¼ of our patients described adverse effects, these were mild and were not a cause of interruption of the treatment.

Abstract no.: P13.16

RESISTANCE OF *H. PYLORI* ISOLATES FROM IRANIAN PATIENTS TO COMMONLY USED FLUOROQUINOLONES

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Introduction: Resistance of *Helicobacter pylori* to antibiotics included in current regimens is a major reason for treatment failure. Therefore, alternative regimens including fluoroquinolones have been developed. In this study we assessed the prevalence of resistance of *H. pylori* isolates from dyspeptic patients to three fluoroquinolones.

Methods: Biopsies from 158 patients with gastric dyspepsia were cultured on selective medium. *H. pylori* isolates were identified by morphology, positive urease, catalase and oxidase activity. Susceptibility of isolates (turbidity: 2 MacFarland) to ciprofloxacin, ofloxcacin and levofloxacin (MIC 1 μg/mL) was determined using disk diffusion method. *H. pylori* isolates with diameter of inhibition zones <20 mm were considered resistant.

Results: The rates of resistance to ciprofloxacin, ofloxcacin and levofloxacin were determined as 48.73%, 62.02% and 43.03%, respectively. Among 158 isolates, 50 (55.6%) exhibited resistance to all three antibiotics and 26 (16.45%) were resistance to two antibiotics.

Discussion: Results of this study indicate that the resistance rates to ciprofloxacin (48.73%), ofloxcacin (62.02%) and levofloxacin (43.03%) increased compared to our previous study, 34.28%, 37.14% and 34.28% respectively. Increase in resistance to ofloxacin was statistically significant. Accordingly, although flouroquinolones have been widely used as an effective drug, prevalence of resistance to these antibiotics is relatively high in Iran and is increasing over time. It could be due to widespread use of these antibiotics for treatment of the genitourinary and respiratory infections and veterinary medicine. Accordingly it is strongly suggested to determine the susceptibility of the *H. pylori* isolates to fluoroquinolones before administration of regimen including these antimicrobial family.

Abstract no.: P13.17

MOLECULAR DETECTION OF CLARITHROMYCIN AND FLUOROQUINOLONES RESISTANCE IN *HELICOBACTER PYLORI* INFECTION, DIRECTLY APPLIED TO GASTRIC BIOPSIES, IN A BRAZILIAN URBAN POPULATION

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Introduction: Antimicrobial resistance is the major factor leading to eradication failure in *H. pylori* (HP) treatment. Molecular tests are useful to detect mutations predictive of clarithromycin and fluoroquinolones resistance. Knowledge of the local prevalence rate of resistance is important to define the best recommended treatment.

Aim: To assess the prevalence of primary resistance of HP to clarithromycin and fluoroquinolones in a southeast urban Brazilian population.

Patients and Methods: 72 HP seropositive patients [65% female, mean age 39 (19–73) years] never treated before to HP were studied. All patients underwent gastroscopy in addition to antrum and corpus biopsies and molecular test GenoType HelicoDR (Hain Life Science, Germany) to detect HP and point mutations in genes responsible for clarithromycin and fluoroquinolone resistance. The molecular procedure was divided into three steps: DNA extraction from biopsy samples, a multiplex amplification with biotinylated primers and a reverse hybridization. The most frequent point mutations involved in resistance to the two antibiotics were evaluated.

Results: Resistance to clarithromycin was detected in nine patients (12.5%) and to fluoroquinolones in eight patients (11.1%). The point mutation A2147G was the most common (77.8%) among resistant strains to clarithromycin. In 50% of the resistant strains to fluoroquinolones, the mutant codon couldn't be identified.

Conclusions: The resistance rates of clarithromycin (12.5%) and fluorquinolones (11.1%) in a large southeast urban population in Brazil show acceptable rates suggesting that these drugs remain appropriated options to first and second line of HP treatment. The molecular test constitutes an adequate diagnostic tool to monitor HP resistance.

Abstract no.: P13.18

THE ROLE OF ACRAB-TOLC EFFLUX PUMP ON ANTIBIOTIC RESISTANCE OF *HELICOBACTER PYLORI* CLINICAL ISOLATES

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Objective: To elucidate the role of AcrAB-TolC efflux pump in multi-drug resistance (MDR) of Hp clinical isolates.

Method: (i) The 10 Hp MDR strains and 10 susceptible strains which are sensitive to 9 kinds of antibiotic were screened from 653 Hp clinical isolates; (ii) The mRNA expression of genes related to AcrAB-TolC efflux pump(hefA, hefB, hefC, hefD, hefE, hefF, hefG, hefH and hefI)were detected by q-PCR; (iii) The mutation of resistance genes which are implicated in Metronidazole(rdxA and frxA), Clarithromycin (23SrRNA), Levofloxacin(gyrA) resistance were detected by gene sequencing, (iv) Influence of efflux pump inhibitors(CCCP and PAβN) on the MDR of Hp were evaluated by testing MIC of antibiotics to Hp.

Results:: (i) There was no high expression of AcrAB-TolC efflux pump mRNA in all the susceptibal strains; 1, 2, 1, 2, 3, 2, 3 and 2 of the MDR strains respectively presented high expression of hefA, hefB, hefC, hefD, hefE, hefF, hefG and hefH mRNA. (ii) The 8 MDR strains which resistant to clarithromycin had mutations in the 23SrRNA gene, All the MDR strains had mutations in the gyrA, rdxA and frxA gene. (iii) The MIC of Clarithromycin was decreased at least 4-fold in 4 MDR strains by PAβN; The MIC of Metronidazole and Clarithromycin respectively were decreased at least 4-fold in 4 and 2 MDR strains by CCCP.

Conclusion: The MDR of *H. pylori* clinical isolates is the result of a combination of the AcrAB-TolC efflux pump system and the resistant genes.

Abstract no.: P13.19

PREVALENCE OF THE POINT MUTATIONS IN 23S RRNA GENE CONFERRING TO THE CLARITHROMYCIN RESISTANCE OF *HELICOBACTER PYLORI* STRAINS – CORRELATION BETWEEN MUTATIONS AND DIFFERENT LEVELS OF RESISTANCE

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Background: The occurrence of clarithromycin resistance among *Helicobacter pylori* (*H. pylori*) strains is the major cause of treatment failure. In regions with high clarithromycin resistance prevalence (e.g.Poland), clarithromycin should be abandoned in empirical treatment. The most prevalent factors contributing to clarithromycin resistance are point mutations in 23SrRNA gene.

Aims: Evaluation of the occurrence of point mutations A2143G and A2142G among clarithromycin resistant *H. pylori* strains and theirs correlation with different levels of clarithromycin resistance.

Materials and Methods: The study included 40 clarithromycin resistant *H. pylori* strains isolated from patients between 2006–2013 in Southern Poland. Clarithromycin resistance was tested by E-test to determine minimal inhibitory concentration (MIC). Point mutations were detected by PCR-RFLP analysis with restrictions enzymes: *Eco31I* and *BbsI*. The occurrence of the mutations was carried out against the reference *H. pylori* ATCC700684strain. The statistical analysis was conducted with the One-sided Fisher's Exact Test at the 0.05 significance level ($p \leq 0.05$).

Results: MICs for clarithromycin ranged from 0.5 mg/L to 256 mg/L. Among analysed strains 57.5% (23/40) exhibited the A2143G mutation, 30% (12/40) – A2142G mutation and 12.5% (5/40) were negative for both mutations. In the A2143G mutants, 96% (22/23) demonstrated low-level resistance to clarithro-

mycin (MIC ≤ 32 mg/L) and 5% (1/23) – high-level (MIC > 32 mg/L), while 58% (7/12) of A2142G mutants had low-level resistance and 42% – high-level. A2143G mutants had statistically significant lower MICs of clarithromycin than A2142G ($p = 0.012$).

Conclusion: Among clarithromycin resistant *H. pylori* strains the most prevalent mutation was A2143G, which was associated with lower level of resistance than A2142G mutation. Fast detection of clarithromycin resistant *H. pylori* strains enables selection of appropriate treatment scheme without clarithromycin.

Abstract no.: P13.20

THE EFFICACY OF SARCANDRA GLABRA EXTRACT ALONE OR COMBINED WITH ANTIBIOTICS AGAINST ANTIBIOTIC-RESISTANT *HELICOBACTER PYLORI* IN VITRO

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Objective: To investigate the effect of sarcandra glabra extract(SGE) alone or combined with antibiotics against drug-resistant *Helicobacter pylori* (*H. pylori*) isolated from clinic.

Methods: The minimum inhibitory concentrations (MICs)of SGE and antibiotics(A-Amoxicillin, C-Clarithromycin, M-Metronidazole, L-Levofloxacin, T-Tetracycline and F-Furazolidone) alone against 20 strains of antibiotic (Clarithromycin, Metronidazole and Levofloxacin) -resistant *H. pylori* were determined by twofold dilution method. The MICs of SGE with antibiotics were determined by agar plate method. The fractional inhibitory concentration indexes (FICI) were calculated to evaluate the combined antibacterial activity. When FICI ≤ 0.5 was defined as synergism, 0.5 < FICI ≤ 1 as accumulation, 1 < FICI ≤ 2 as independence and FICI > 2 as antagonism.

Results: The MIC of SGE against 20 strains of antibiotic-resistant *H. pylori* were 2.5–0.625%. The FICI in 6 groups of SGE with antibiotics against 10 antibiotic -resistant *H. pylori* strains were respectively [Form: Drugα+ Drugβ = FICI (NO. of strains)]: (i) S+A ≤ 0.5 (10), >0.5(0); (ii) S+M ≤ 0.5 (7), 0.5–1 (3), >1 (0); (iii) S+L ≤ 0.5 (6), 0.5–1 (4), >1 (0); (iv) S+F ≤ 0.5 (10), >0.5 (0); (v) S+T ≤ 0.5 (10), >0.5 (0); (vi) S+C = 0.5 (8), 0.5–1 (2), >1 (0).

Conclusion:

1. SGE have bacteriostasis against antibiotic-resistant *H. pylori* strains.
2. SGE combined with amoxicillin, tetracycline or furazolidone have synergistic action. SGE combined with Clarithromycin, Metronidazole or Levofloxacin have additivity action.
3. Supplementation with SGE during *H. pylori* eradication therapy maybe improve antibiotic-resistant *H. pylori* eradication.

Abstract no.: P13.21

PREVALENCE OF A2143G POINT MUTATION FOR CLARITHROMYCIN RESISTANCE AT THE FIRST DIAGNOSIS OF *H. PYLORI* INFECTION IN SOUTHERN ITALY

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Background: Among the point mutations conferring clarithromycin resistance, only A2143G has been shown to have a strong impact on the failure of the different first line regimens for *H. pylori* eradication. Therefore, its detection may be the most useful tool for clarithromycin exclusion from the first line treatment.

Aim: To detect A2143G prevalence at the first diagnosis of *H. pylori* infection in an area at high clarithromycin resistance.

Methods: Fifty consecutive patients (19 M and 31 F, age range 46–66) undergoing esophagogastoduodenoscopy for upper gastrointestinal symptoms were recruited. In all histology and stool antigen test (HpSA) were performed and the positivity for at least one test was used as inclusion criterion. In all patients A2143G point mutation was detected by real time polymerase chain reaction on paraffin-embedded samples after bacterial DNA isolation.

Results: *H. pylori* DNA was isolated from all patient samples. The concordance with histology was found in 46/50 (92%). A2143G point mutation was found in 11/50 (22%) patients.

Conclusions: The present study suggest that: (i) The search of *H. pylori* DNA in gastric specimens has a good agreement with histology and could be considered as a diagnostic tool even for histology-negative doubtful cases; (ii) The prevalence of A2143G reflects that of clarithromycin resistance in our geographic area; (iii) Mutation detection at first diagnosis could address therapeutic choice by excluding clarithromycin based first-line regimens.

Abstract no.: P13.22

EVALUATION OF *HELICOBACTER PYLORI* FIRST LINE ERADICATION THERAPY (PPI/AC) IN ELDERLY PATIENTS – EVALUATION OF CLARITHROMYCIN RESISTANT RATE AND ERADICATION RATE

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Background: Sixty-five years or older person accounts for 24.1% of the population in Japan. Therefore, a triple therapy which consists of amoxicillin (AMPC), clarithromycin (CAM), and a proton pump inhibitor (PPI) [PPI/AC] has been commonly used for the first line eradication regimen of *Helicobacter pylori* (*H. pylori*) in many elderly patients. *H. pylori* related chronic gastritis was approved and covered by national health insurance in February 2013. So, an increase of *H. pylori* eradication cases in elderly patients is expected.

Aim: To evaluate the influence of CAM resistance in *H. pylori* positive elderly patients treated with PPI/AC regimen.

Methods: The subjects were 202 *H. pylori* positive patients consist with 52 patients aged over 65 years and 150 patients aged under 65 years. *H. pylori* culture and CAM susceptibility test were performed using gastric biopsy specimens. All patients were treated with PPI/AC regimen. Eradication was confirmed with ^{13}C-urea breath test.

Results: The eradication rate were 80.2% (162/202) for all patients, 73.1% (38/52) for aged over 65 years group, 82.7% (124/150) for aged under 65 years group, respectively. CAM-resistant rate for *H. pylori* were 17.8% (36/202) for all patients, 23.1% (12/52) for aged over 65 years group, 16.0% (24/150) for aged under 65 years group, respectively.

Conclusion: Since CAM-resistant rate for *H. pylori* in elderly patients are higher than in young patients, the eradication rate in elderly patients are lower than in young patients.

Abstract no.: P13.23

DRUG RESISTANT *H. PYLORI* STRAINS ISOLATED IN MONGOLIA

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Background: The resistance of *H. pylori* to the recently available antibiotic treatment regimens has been a growing problem.

Objective: To evaluate the presence and prevalence of antibacterial resistance in *H. pylori* in Mongolia.

Material and Method: Gastric biopsy specimens were used for *H. pylori* culture. The susceptibilities of the *H. pylori* isolates to clarithromycin, metronidazole, amoxicillin, tetracyclin, nitrofurantion and erytromycin were examined by Etest strip. In addition, GenoType Helico DR which employs reverse hybridisation was used to confirm the presence of *H. pylori*, and detection of mutations conferring resistance to clarithromycin and fluoroquinolones.

Result and Discussion: The 152 isolates were available for antimicrobial susceptibility testing. Resistant rate to metronidazol is in 68.4%, than to clatritromycin is 35%, and amoxicillin is 33%. Of all *H. pylori* strains, resistance for 2 drugs was observed in 34.5% and that for 3 drugs were observed in 17.7% of isolates. *H. pylori* resistance for 4 or 5 drugs was detected in 7.1%. All 6 agents resistance observed in one strain. The 23S gene mutation observed in 37,8%, gyrA gene mutation of codon 87 in 10.5%, and codon 91 mutation in 12.6% (A2147G)

Conclution: The prevalence of resistance of *H. pylori* is very high to metronidazole, moderate to clarithromycin, multidrug resistant strains to second choose treatment are more frequently found. *H. pylori* antibiotic resistant strains frequently have mutations in the 23S rRNA gene and gyrA gene.

Abstract no.: P13.24

A MOLECULAR GENETICS-BASED APPROACH FOR THE DETECTION OF CLARITHROMYCIN AND FLUOROQUINOLONE RESISTANT *H. PYLORI* INFECTION

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Introduction: Molecular assays provide an alternative to standard *H. pylori* culture and antimicrobial susceptibility testing. Single point mutations in the *H. pylori* rrl gene encoding the 23S ribosomal RNA confer resistance to clarithromycin. Mutations in the gyrA gene encoding the A subunit of DNA gyrase confer resistance to fluoroquinolones.
Aim: To evaluate the performance of the GenoType HelicoDR assay for the detection of *H. pylori* and antibiotic resistance compared to standard culture and antimicrobial susceptibility testing.
Methods: Biopsies from patients positive for *H. pylori* infection by the Campylobacter-like organism (CLO) test were cultured for antimicrobial susceptibility testing using Etests (Biomerieux). Biopsy DNA was analysed for resistance-mediating mutations using the GenoType HelicoDR assay (Hain Lifesciences).
Results: *H. pylori* DNA was detected in all of the 49 samples tested from CLO-positive patients using the GenoType HelicoDR assay. The culture success rate was 55% (27/49). Genetic resistance to clarithromycin was 47% (23/49). 22 of the clarithromycin-resistant strains had the A2147G mutation, while 1 had the A2146G mutation. Genetic resistance to fluoroquinolones was 12% (6/49). All fluoroquinolone resistant strains were mutated at position 91 of the gyrA gene. Of the 27 samples from which both culture and molecular test results were available, the concordance in antimicrobial susceptibility data was 85% (23/27).
Conclusion: Overall genetic resistance rates for clarithromycin and fluoroquinolones in our patient cohort were 47% and 12% respectively. Further studies are required to investigate the impact of genetic resistance on treatment outcome to assess the potential use for molecular assays in the clinic.

Abstract no.: P13.25

A NOVEL METHOD TO FACE LOW MUCOSA PENETRATION AGAINST *HELICOBACTER PYLORI*

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Introduction: *Helicobacter pylori* is known as the major cause of gastric ulcerations. A common treatment is using multiple antibiotic therapy, due to the low permeability of drugs into the gastric mucosa. This method of treatment imposes patients to the various side effects and antibiotic resistance. In the current study, cinnamon (*Cinnamomum zeylanicum*) was used as an herbal medicine to evaluate its antibacterial activity against *H. pylori*.
Materials and Methods: Biopsy samples were obtained from endoscopy candidates who referred to Fayazbakhsh hospital during 2013. All samples were homogenized immediately after they received and cultured on supplemented blood agar. All plates incubated at micro-aerophilic condition and 37°C for 72 hours. *H. pylori* identification was done by Gram staining and biochemical tests like urease, oxidase and catalase activity. Essential oil (EO) of cinnamon was prepared and analyzed using GC-MS. Cinnamaldehyde was detected as the major component. o/w nanoemulsions were then prepared and optimized using sonication method and 5% (EO), Tween80 and Span80 as the surfactants. The antibacterial effect of EO and Cinnamaldehyde against *H. pylori* was then surveyed using MIC determination and disk diffusion assays.
Results and Conclusion: According to the results of antibacterial assays the best MIC value was observed for EO with MIC 0.14 mg/mL, while this value was reduced to 0.06 mg/mL for nanoemulsion. Cinnamaldehyde performed better than EO in case of disk diffusion assays, where the inhibition zone was 54 mm and 62 mm for 10 µL/disk and 20 µL/disk, respectively.

Abstract no.: P13.26

COMPARISON OF ANTIMICROBIAL ACTIVITY OF OMEPRAZOLE AND LANSOPRAZOLE AGAINST *H. PYLORI*

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Aim: Proton pump inhibitors (PPIs) have been regarded as effective anti-*H. pylori* components when used in combination with the currently used antibiotics. The study aimed to compare the anti-*H. pylori* activities of omeprazole with lansoprasole.
Methods: 105 *H. pylori* isolates from dyspeptic patients were recruited. Serial dilutions of omeprazole (128, 64, 32, 16) and lansoprazole (16, 8, 4, 2) were prepared in DMSO. Ten microliter of each dilution was impregnated into blank disks on the surface-inoculated blood plates. Plates were incubated at 37°C and microaerophilic conditions and diameter of inhibition zones was recorded after 3–5 days.
Results: The MICs for omeprazole and lansoprazole were determined as 32 and 8 µg/mL, respectively. Among the 105 *H. pylori* isolates 93 (88.57%) were sensitive to omeprazole and 94 (89.52%) to lansoprazole. The size of inhibition zones was 14–65 (mean 39.5 mm).
Discussion: Omeprazole and lansoprazole were similarly effective against most of the *H. pylori* isolates. However, 12 strains were resistant to omeprazole and 11 to lansoprazole. From these PPIs resistant strains 53% also showed resistance to at least 5 currently used antibiotics. Future study could focus on the *H. pylori* strains that showed resistance to these PPIs.

Abstract no.: P13.27

THE STANDARD TRIPLE THERAPY WAS NOT EFFECTIVE FOR PATIENTS WHO HAD 23S RIBOSOMAL RNA MUTATED *HELICOBACTER PYLORI*

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Background: Proton pump inhibitor and two types of antimicrobial agents, amoxicillin, and clarithromycin have been widely used in the eradication of *Helicobacter pylori*. However, antibiotic resistant strain has been rapidly increased as an important factor for the failure of eradication. Previously, special attention was given to the mechanism of clarithromycin resistance, and mutations of A2143G or A2144G in the bacterial 23S ribosomal RNA (23S rRNA) gene were well established with the relation of clarithromycin resistance.
Patient and Methods: Patients was examined by *H. pylori* PCR and mutation at 23S ribosomal RNA. Positive *H. pylori* PCR without 23S rRNA mutation was eradicated by standard triple therapy. But, positive *H. pylori* PCR with 23S rRNA mutation was eradicated by standard triple therapy or concomittent therapy with amoxicillin, proton pump inhibitor, clarithromycin and metronidazol or quadruple therapy with bismuth, proton pump inhibitor, tetracycline and metronidazol.
Result: *H. pylori* PCR positive was 295/796. 23S rRNA mutatation was 69/295. The eradication rate of *H. pylori* for the point mutated group with standard triple therapy was 34.4% (10/29), and significantly lower than those of wild type group which are 95.7% (113/118), concomitant therapy group which are 100%(6/6) and quadruple therapy group which are 85.7%(6/7), respectively ($p = 0.005$)
Conclusions: When 23S rRNA point mutation was positive, the standard triple therapy was not effective. We should consider the alternative regimen for the 23S rRNA point mutation group and survey the eradication rate of alternative regimen. We'll accumulate more data about eradication rate of alternative regimen of *H. pylori*.

Abstract no.: P13.28

INVESTIGATION OF ANTIMICROBIAL ACTIVITY TO DETERMINE MIC VALUE OF CINNAMON BARK OIL AGAINST *HELICOBACTER PYLORI*

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Aim: To determine MIC-value of cinnamon-bark-oil in comparison with clarithromycin, also to investigate the effects of different parameters on antimicrobial activity of cinnamon-bark-oil.

Method: Agar dilution method was used to determine the MIC-value of clarithromycin and cinnamon bark oil(Sigma) by adopting CLSI recommendation and also different parameters were performed to investigate the effects on bacterial growth due to the difficult differentiation of *H. pylori* NCTC 11637 standart strain growth on cinnamon-bark-oil containing agar plates.

Serial dilutions of cinnamon-bark-oil were prepared in range of 1–1000 μg/mL. MHA with both 5% and 10% sheep blood containing various concentrations of cinnamon-bark-oil were prepared. Inoculum concentration of *H. pylori* was adjusted to McFarland No2, No3 and No4. Suspensions were inoculated 3 and 5 μL by spot and spreading directly onto agar plates and incubated at 37°C for 72 hours under microaerophilic conditions.

All assays were performed in triplicate.

Results: MIC-value of cinnamon bark oil and clarithromycin were found 8 and 0.125 μg/mL, respectively.No significant difference was found for colony growth by different McFarland scales and inoculum amounts. Because of the transparent and fragile colonies of *H. pylori,* spreading bacterial suspension directly onto agar plates was better to differantiate colony growth. Although, the different inoculum concentrations and amounts didn't effect the MIC-value, much more colonies were observed in McFarland3 and 4 in comparison to McFarland 2.

Conclusion: These results indicate that McFarland3 and/or 4 should be used to evaluate and to obtain the best growth of *H. pylori* for the antimicrobial activity of the cinnamon-bark-oil as an essential oil; and also spreading plate methodology could be considered instead of spots for exact decision of inhibition concentration.

Abstract no.: P13.29

INCREASE IN THE RESISTANCE RATES OF *H. PYLORI* ISOLATES AFTER 5 YEARS

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Aim: The aim of study was to examine the antibiotic resistance of *H. pylori* isolates from Iranian dyspeptic patients and compare the rates with those obtained 5 years ago.

Methods: *H. pylori* isolates were obtained from 158 patients (137 with gastritis, 19 peptic ulcer and 2 with precarcerous lesions), 83 female and 75 male (19–86 years, mean age 45.5 years) using selective blood agar and microaerophilic incubation. Disk diffusion method was used to evaluate resistance of isolates to metronidazole, clarithromycin, tetracycline, amoxicillin and furazolidone with MICs (μg/mL) of 8, 2, 0.5, 1 and 1, respectively.

Results: Resistance rates were estimated basis of diameter of inhibition zone of ≥20 mm for all antibiotics except furazolidone (≥13 mm). Resistance rate of metronidazole was 81.64, clarithromycin %30.37, tetracycline %42.40, amoxcillin %27.21 and furazolidone %19.62.

Discussion: When compared with the results of our previous study in 2008, resistance rates to all the currently used antibiotics showed a significant increase. No significant difference was found between antibiotic resistance age, gender and gastric diseases.

P14 Immunity, Animal Models & Vaccines

Abstract no.: P14.01

IDENTIFICATION OF *H. PYLORI* EPITOPES RESPONSIBLE FOR HOST IMMUNO-RESPONSE MODULATION THROUGH ORF-FILTERED PHAGE DISPLAY LIBRARIES AND INTERACTOME-SEQUENCING

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To elucidate the molecular mechanisms involved in persistency/latency of the *H. pylori* infection or in its progression towards serious diseases, it is necessary to analyze the host pathogen interaction in vivo. The circulating antibody repertoire represents an important source of diagnostic information, serving as biomarker to provide a "disease signature"; its analysis can lead to the identification of *H. pylori* epitopes responsible for host immuno-response modulation.

Here we propose a discovery-driven approach that couples "phage display" and deep sequencing. This approach provides a simple procedure for identifying novel antigens, by screening gDNA libraries, created from the pathogen genome, directly with sera from infected patients.

Three phage display libraries from three *H. pylori* strains (HP-26695, HP-B128 and HP-SS1) have been constructed by using β-lactamase ORF selection vectors (Di Niro et al., 2010). Genomic DNA was sonicated, fragments cloned into the filtering vector, after transformation libraries of 1x106 clones were obtained and sequenced by 454 technology, showing that 93% of the CDSs were represented, therefore being representative of the whole *H. pylori* antigenic ORFeome.

Finally putative antigens were selected from libraries using sera from patients affected by *H. pylori* presenting increasing degrees of infection: (i) autoimmune gastritis and pernicious anemia; (ii) gastric adenocarcinoma; (iii) MALT lymphoma. The results show that the diversity of the libraries obtained after selection is significantly reduced. Furthermore, individual ranks, for each infection condition, have been compared highlighting the pattern of putative antigens, shared by all the conditions, and some that can distinguish the different stages of infection.

Abstract no.: P14.02

CHRONIC *HELICOBACTER PYLORI* INFECTION CAUSES SERUM IRON STORAGE DEPLETION AND ALTERS LOCAL IRON GENE EXPRESSION IN INS-GAS/FVB MICE (*MUS MUSCULUS*)

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Iron deficiency anemia affects >500 million people, and is linked to impaired cognitive development in children. *Helicobacter pylori* also affects a substantial proportion of the world's population. Previous studies suggest that a causative relationship exists between *H. pylori* pathogenicity and iron deficiency. We examined the effect of *H. pylori* infection on iron deficiency and brain iron homeostasis in a mouse model. Two replicates of INS-GAS/FVB male mice were dosed with *H. pylori* (*Hp*) strain SS1 or sham dosed at age 7–9 weeks. Mice were necropsied at 25–27 weeks post infection. Serum ferritin was lower in *Hp*-infected mice than uninfected mice ($p < 0.0001$). Infected mice had a lower red blood cell count and hematocrit ($p < 0.001$). Mean cellular volume was increased in infected mice ($p < 0.0001$), as was reticulocyte % ($p < 0.01$), and erythropoietin ($p = 0.001$). Gastric expression of hepcidin was downregulated in *Hp* SS1 infected mice ($p < 0.05$). Expression of brain divalent metal ion transporter ($p = 0.01$) was upregulated in *Hp* SS1 infected mice, while expression of brain derived neurotrophic factor 4 (synaptic plasticity marker) was downregulated in infected mice, both consistent with brain iron deficiency. Our data indicate that infection with *Hp* SS1 causes depletion of serum iron stores and deregulated gastric and brain gene expression related to both iron metabolism and synaptic plasticity. Blood analysis was consistent with anemia due to blood loss. Ongoing studies seek to further define the relationship between *H. pylori*, iron deficiency, anemia, and cognitive function.

Abstract no.: P14.03

ORAL ADMINISTRATION OF TRANS10, CIS12 CONJUGATED LINOLEIC ACID (CLA) IN MICE INCREASES IMMUNE CELL ABUNDANCE IN THE ADIPOSE TISSUE BUT NOT IN THE INTESTINE

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Oral administration of trans10, cis12 conjugated linoleic acid (CLA) provokes an accumulation of macrophages in the adipose tissue (Poirier et la, Diabetes 2006). Here, we used this model: (i) to assess the components of this immune response in adipose tissue, (ii) to test whether the compound affect gut immunity and permeability and (iii) to evaluate the resilience of adipose tissue and intestine with disruption of treatment.

Methods: Immune cell abundance and phenotype were assessed by gene expression analysis immunohistochemistry and flow cytometry in adipose tissue, jejunum and colon of mice receiving daily gavage of CLA for 7 days and after 9 days with no gavage.

Results: Macrophages but also T-lymphocytes accumulated in adipose tissue with CLA treatment. Phenotypic analysis revealed the prevalence of M2 anti-inflammatory macrophages. Immune cell infiltration was fully reversible after 9 days. In contrast to adipose tissue, both jejunum and colon displayed no alteration in the expression of macrophage and T-lymphocyte markers after 7 CLA gavages. However, a decreased expression of genes encoding tight junction proteins (claudin and occludin) was observed.

Conclusion: The molecular and cellular mechanisms by which oral administration of CLA induce a marked immune response in the adipose tissue remain unknown. Here, we show that this response is appropriate, as suggested by the reversibility of the cellular alterations enlightening an unexpected resilience of adipose tissue. Moreover, we propose that part of the effect of CLA could be mediated by CLA-induced increased intestinal permeability.

P15 Probiotics

Abstract no.: P15.01

A STANDARD 7 DAY CLARITHROMYCIN BASED FIRST LINE THERAPY ENRICHED WITH A MIX OF *BACILLUS COAGULANS* LACTOFERRIN AND FRUCTOOLIGOSACCHARIDES IS EQUIVALENT TO SEQUENTIAL THERAPY IN TERMS OF *H. PYLORI* ERADICATION

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Background: Previous studies showed a role of Lactoferrin, pre and probiotics in increasing *H. pylori* eradication rate. In Italy, the best first line regimen is the 10-day sequential therapy. Whether adding all those adjuvants to a standard therapy may exert a positive effect, possibly decreasing the duration of the therapy is not known.
Methods: 300 age and sex-matched patients were randomized into 3 different schemes: (i) Lansoprazole 15 mg/bid, Amoxicillin 1 g/bid, Clarithromycin 500 mg/bid for 7 days (LAC); (ii) sequential Lansoprazole 15 mg/bid plus Amoxicillin 1000 mg/bid for 5 days, followed by Lansoprazole 15 mg/bid, Clarithromycin 500 mg/bid and Tinidazole 500 mg/bid for 5 days (LACT); (iii) Lansoprazole 15 mg/bid, Amoxicillin 1 g/bid, Clarithromycin 500 mg/bid for 7 days enriched with a mix of Lactoferrin, Fructooligosaccharides and Bacillus Coagulans/tid for 15 days (LAC-LFB). Eradication was confirmed by UBT. Compliance and adverse effects were also assessed.
Results: Eradication rates were: LAC 72%, LACT 79.2% and LAC-LFB 85%. Eradication rates were higher in LAC-LFB compared to LAC ($p < 0.025$) and similar in LAC-LFB compared to LACT ($p = 0.272$). Interestingly, the occurrence of side effects was significantly lower in the group of LAC-LFB.
Conclusions: A mix of Lactoferrin, Fructooligosaccharides and Bacillus Coagulans significantly increases the eradication rate of a standard clarithromycin based triple therapy making it comparable to the sequential therapy. The lower duration of the antibiotic therapy and the reduced occurrence of antibiotic-related side effects make LAC-LFB a good alternative to sequential therapy.

Abstract no.: P15.02

SUPPRESSION OF GUT MICROBIOTA DYSBIOSIS AND ALLEVIATION OF SEVERE DIARRHEA BY INGESTION OF PROBIOTIC *BIFIDOBACTERIUM BIFIDUM* YIT 10347 IN JAPANESE RECIPIENTS OF *HELICOBACTER PYLORI* ERADICATION THERAPY

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Background and Aim: A main cause of diarrhea following *Helicobacter pylori* eradication therapy is gut microbiota dysbiosis. We conducted a randomized double-blind placebo-controlled clinical trial to examine the effect of probiotic *Bifidobacterium bifidum* YIT10347 on *H. pylori* eradication, diarrhea, and gut microbiota dysbiosis.
Methods: Participants were 228 Japanese patients who were randomized into an active group or placebo group, and ingested 100 mL of either fermented milk containing *B. bifidum* YIT10347 (active group) or non-fermented milk (placebo group) once daily for 17 weeks. Triple therapy (lansoprazole 30 mg bid, amoxicillin 750 mg bid, clarithromycin 200 mg bid) was treated at week 8 for 1 week to eradicate *H. pylori* (HpBF study), and side effects and rate of eradication were evaluated. Gut microbiota of 16 participants per group were analyzed by 16S rDNA metagenomic sequencing and the UniFrac index was used to evaluate gut microbiota dysbiosis.
Results: *H. pylori* eradication rate and the occurrence of side effects did not significantly differ between the groups, except that the occurrence of severe diarrhea ≥4 days was significantly lower in the active group. Gut microbiota dysbiosis occurred in both the groups, but the increase in the UniFrac index was significantly suppressed in the active group. Recovery of gut microbiota was significantly earlier in the active group (2–4 weeks than in the placebo group (8 weeks).
Conclusion: Ingestion of probiotic *B. bifidum* YIT10347 suppressed gut microbial dysbiosis and alleviated severe diarrhea in Japanese recipients of *H. pylori* eradication therapy.

Abstract no.: P15.03

IMPROVE ERADICATION RATE OF STANDARD TRIPLE THERAPY BY ADDING BISMUTH AND PROBIOTIC SUPPLEMENT FOR *H. PYLORI* TREATMENT IN THAILAND

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Objective: Standard triple therapy for *H. pylori* eradication is no longer effective in many countries including Thailand. This study designed to evaluate efficacy of adding bismuth and probiotic to standard triple therapy for *H. pylori* eradication in Thailand.
Method: This prospective single center study was done. *H. pylori* infected gastritis patients were randomized to 7- or 14-day standard triple therapy plus bismuth with probiotic or placebo. Treatment regimen consisted of bismuth subsalicylate (524) 2 tab twice daily, lansoprazole (30 mg) twice daily, amoxicillin 1 g twice daily and clarithromycin MR 1 g once daily. Probiotic bacteria were composed of *Bifidobacterium lactis, Lactobacillus acidophilus* and *Lactobacillus paracasei*. Placebo was drinking yogurt without probiotic. CYP2C19 genotyping and antibiotic susceptibility tests were done. *H. pylori* eradication was evaluated by ^{13}C-UBT 2 weeks or more after treatment.
Results: 100 subjects were enrolled (25 each to 7- and 14-day regimens with probiotic or placebo). Antibiotic susceptibility testing showed 36.7% metronidazole and 1.1% of clarithromycin resistances. CYP2C19 genotyping revealed 40.8% RM, 49% IM and 10.2% PM. Eradication rate with 7- or 14 regimens with probiotic achieved eradication rate of 100%. Interestingly, side effects with bitter taste in 7-day regimen with probiotic was significant less than 7-day regimen with placebo (40% vs 64%; p –value = 0.04).
Conclusion: 7-day standard triple therapy plus bismuth and probiotic provided excellent cure rate (100%) regardless of CYP2C19 genotype with less adverse reactions in low clarithromycin resistance area. 7-day standard triple therapy can return to clinical practice by adding bismuth and probiotic.

Abstract no.: P15.04

H. PYLORI-ERADICATION: EFFICACY AND SAFETY OF PROBIOTIC

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Aim: To evaluate the efficacy and safety of synbiotic with LAB stain Enterococcus faecium L-3 compared with prebiotic and placebo for *H. pylori* eradication in duodenal ulcer (DU) patients.
Methods: Randomized double-blind placebo-controlled trial. 81 *H. pylori*-positive patients with DU in remission were randomly assigned to three groups: Group A received symbiotic (LAB - Enterococcus faecium L-3 10^6–7 CFU/g, pectin, soy protein hydrolyzate, Laminaria saccharina), group B - prebiotic (pectin, soy protein hydrolyzate, Laminaria saccharina), group C-placebo. Patients took three pills t.i.d. 8 weeks.
Results: *H. pylori* eradication rates for the groups A, B, and C were 38% (11 of 29), 8.7% (2 of 23) and 10% (3 of 25), respectively. Synbiotic had showed a higher eradication rate than prebiotic ($\chi^2 = 5.85$, $p = 0.0156$) or placebo ($\chi^2 = 4.61$, $p = 0.0317$). Clinical or endoscopic relapses of UD or chronic gastritis were observed in 14 patients in group A, 6 patients in group B and 8 patients in group C. Though *H. pylori* was eradicated, relapses still occurred in some cases. Attributive relapse risk was 0.48, 0.26 and 0.28, respectively. Relapse risk ratio was 2.45 (symbiotic vs placebo). No cases of enterococcus colonization of gastric mucosa were revealed by PCR with E. faecium specific primers.
Conclusion: Monotherapy with synbiotic based on Enterococcus faecium is not enough effective for *H. pylori* eradication but more effective then prebiotic or placebo for *H. pylori* eradication in DU patients. Monotherapy with symbiotic increases the risk of peptic ulcer relapse, indicating *H. pylori* is the major cause but not the only one.

Abstract no.: P15.05

ANTI-*HELICOBACTER PYLORI* EFFECT OF FERMENTED RED GINSENG AND *LACTOBACILLUS PLANTARUM*

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Background/Aims: The Korean red ginseng or *L. plantarum* inhibits inflammatory change due to *H. pylori* infection. The authors wonder how potent anti-*H. pylori* effects of *L. plantarum* fermented ginseng and if synergy effect of administration *L. plantarum* and *L. plantarum* fermented ginseng at same time in vivo.

Materials and Methods: IL-10-deficient mice and Mongolian gerbil mice were divided into only infection group and other group that received *L. plantarum,* red ginseng or fermented red ginseng extracts. After infection, histopathologic scoring, iNOS, COX-2, pERK, IL-6 and so on were determined.

Results: Histopathologic scoring was superior in group of *L. plantarum,* red ginseng or fermented red ginseng. Other proinflammatory cytokines were suppressed by *L. plantarum,* red ginseng extracts or fermented red ginseng extracts. Fermented red ginseng was better than red ginseng. Furthermore, there was synergy effect between *L. plantarum* and fermented red ginseng.

Conclusions: The rapid spread of resistant *H. pylori* strains caused by antibiotics therapy, the addition of a fermented food, such as fermented red ginseng, containing *L. plantarum* to the conventional antibiotic treatment of Helicobacter infection should be considered.

Abstract no.: P15.06

EFFICACY OF DIFFERENT PROBIOTICS AS ANTIHELICOBACTER MEDICATIONS IN VITRO

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Background: It is known that addition of different probiotics to the standard eradication therapy can increase eradication rate. According to Maastricht-IV (2012): "certain probiotics and prebiotics show promising results as an adjuvant treatment in reducing side effects". But also probiotics can have any other effects, eg. positive influence of probiotic on the human immune system or by the direct inhibition of *H. pylori* by bacteriocines of probiotic strain.

The Aim: To analyze the efficacy of different probiotics as antihelicobacter medications in vitro.

Methods: 14 strains of *Helicobacter pylori* were successfully cultivated from dyspeptic patients. Incubation was made in standard conditions for *H. pylori*. We used two variants of probiotic medications: 1st contain Enterococcus faecium strain L-3, 2nd - lyophilisate cultural fluid of Bacillus subtilis. The studied probiotic medications were dissolved in distilled water in part 1:100 and were added in a cup with an agar with different *H. pylori* strains. The assessment of growth of *H. pylori* was analyzed after 6–7 days. Statistical estimation was performed in Excel for Windows XP.

Results: Inhibition of grow of *H. pylori* was in 50% cases with Bacillus subtilis and in 78.6% with Enterococcus faecium strain L-3.

Conclusion: These results can be associated with direct inhibition of *H. pylori* by probiotics. But it is necessary to do more researches to confirm this hypothesis.

P16 Other Helicobacters

Abstract no.: P16.01

AN EPITHELIAL CELL XENOGRAFT MOUSE MODEL TO STUDY THE EFFECTS OF THE CYTOLETHAL DISTENDING TOXIN SUBUNIT CDTB OF *HELICOBACTER HEPATICUS*

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The Cytolethal Distending Toxin (CDT) of *Helicobacter hepaticus* plays a key role in inflammation and the development of liver cancer in mice via its active subunit CdtB. The aim of the present study is to evaluate the direct effect of the CdtB on tumoral development.

We developed several epithelial cell lines allowing the inducible expression of the CdtB of *H. hepaticus*. The *cdtB* gene fused at its 3′ end to three repeats of the influenza hemagglutinin epitope (3HA) was cloned into a plasmid having the tetracycline inducible TRE promoter. The transfer of the *cdtB*-3HA sequence in HT29 human colon adenocarcinoma and Hep3B hepatocellular carcinoma cell lines was achieved by lentiviral transduction and transduced cells were selected in the presence of puromycin. HT29 transduced cell lines (red fluorescent protein or *cdtB-3HA*) were engrafted into NSG immunodeficient mice (n = 15) and the tumoral development was followed over time by measuring the tumor size. After successful engraftment, mice were treated with doxycyclin. Preliminary results revealed good tumor growth in control RFP mice while the tumor growth was delayed in CdtB mice when compared to control cells (3 vs 50 mm^3 per day). These results were confirmed by the tumor weight at necropsy: 0.114 versus 1.414 g in CdtB and RFP mice, respectively. Preliminary histology results revealed an increased in caspase 3 expression in response to the CdtB. New engraftments are in progress into NSG immunodeficient mice (n = 40). This cell xenograft mouse model constitutes a new way of exploring the CdtB effects of *H. hepaticus*.

Abstract no.: P16.02

HELICOBACTER PULLORUM ISOLATES IN FRESH CHICKEN MEAT – PHENOTYPIC AND GENOTYPIC FEATURES

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This study reports sequencing of four *Helicobacter pullorum* strains isolated from fresh chicken meat, using a membrane filtration method. Whole-genome sequencing (WGS) using Illumina technology (MiSeq) followed by *de novo* assembly using the Velvet software was performed. Sequence contigs were aligned and ordered against the reference scaffolds of strain MIT 98–5489 using MAUVE. The DnaSP software was applied to identify genomic regions with high SNP density. Antibiotic susceptibility testing was performed by agar disc diffusion.

Genomes were extrapolated to vary from 1.7 to 2.1 Mb (GC content of ~34%), revealing >98% similarity (on core-genome) with a mean number of nucleotide differences of 22031.5 (SE ± 91.9). DnaSP analysis revealed some high polymorphic regions, which were comprised mostly of hypothetical proteins, restriction-modification enzymes, outer membrane proteins and a putative cytotoxin. A cryptic plasmid of 4,149 bp was found in one isolate.

The four strains were resistant to ciprofloxacin, one was also erythromycin resistant and another was tetracycline resistant. Ciprofloxacin resistance was associated with a Thr→Ile substitution at codon 87 of GyrA; erythromycin resistance was associated with the transition A2075G in 23S rRNA gene; tetracycline resistance was associated with a single transversion A926T in 16S rRNA gene (all according to *H. pylori* numbering).

The WGS approach revealed important features of *H. pullorum,* such as the molecular basis of antibiotic resistance, and a high similar core-genome marked by some high polymorphic regions covering genes with putative roles on host adaptation. Taken together, these results emphasize the bacterium's role as a foodborne pathogen.

Abstract no.: P16.03

NOVEL *HELICOBACTER* SP. ISOLATED FROM COMMON MARMOSETS (*CALLITHRIX JAACHUS*)

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Purpose bred common marmosets from domestic sources housed in a U.S research facility, and used in multiple drug discovery programs, were noted to have a high incidence of spontaneous inflammatory bowel disease and sporadic cholecystitis and cholangiohepatitis. Inflammatory infiltrates increased in incidence and severity with age. Because *Helicobacter* spp. have been linked to gastrointestinal diseases, samples from the gastrointestinal tracts of 39 marmosets were screened for *Helicobacter* spp. by culture and PCR. *Helicobacter* sp. was frequently noted in marmosets; 26% of the marmosets were positive for helicobacters by culture, and 49% were positive by PCR. Older animals (age 6–10) had a higher helicobacter prevalence rate (61%) compared to younger animals (age 3–5), which had a 25% prevalence rate of *Helicobacter* sp. By fluorescence in situ hybridization, helicobacters were also detected in the cecum and colon tissue sections. Seventeen strains of Helicobacter sp. were isolated by culture from various samples including stomach, jejunum, colon, cecum, feces, liver and gall bladder. The *Helicobacter* sp. were catalase, urease positive, oxidase negative and had fusiform morphology; 16S and 23S rRNA sequence analysis revealed that all the Helicobacter sp. had similar sequences, which clustered as a novel *Helicobacter* sp. closely related to *H. sanguini* (96%), a species isolated from cotton-top tamarins. The whole genome sequence of one of the liver isolates MIT 09–6949 has a 1.9 Mb genome length with a 41% GC content. These findings add to the increasing number of animal species with gastrointestinal disease in which novel enterohepatic helicobacters have been isolated.

Abstract no.: P16.04

HEPATOBILIARY TRACT CANCER AND SEROPOSITIVITY TO *HELICOBACTER SPP.* IN THE ATBC STUDY

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Background: We recently found seropositivity to several *H. pylori* proteins to be associated with biliary tract cancers within the prospective Finnish Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) study, although evidence for other Helicobacter species (*H. bilis* and *H. hepaticus)* has also been described previously. To detect antibodies to other *Helicobacter spp* and to assess their species specificity we explored multiplex serology based on membrane extracts of *H. pylori, H. hepaticus,* and *H. bilis*.

Methods: Fluorescent bead-based (Luminex) multiplex serology used 15 recombinantly expressed GST-*H. pylori*-tag fusion proteins and membrane extracts of *H. pylori, H. hepaticus* and *H. bilis* as antigens. Sera of 64 biliary and 122 liver cancer patients and 224 age-matched controls (ATBC study) were analyzed.

Results: Antibody reactivities to biliary tract cancer-associated *H. pylori* proteins Omp, UreA, HP0231 and HP0305 could specifically be blocked by *H. pylori* membrane extract. In addition to *H. pylori,* the prevalence of antibody reactivities to membrane extracts of *H. hepaticus* and *H. bilis* were more common in biliary tract cancer patients compared to controls. Antibodies to *H. bilis* reached statistical significance in association with gallbladder cancer (OR: 3.30, 1.06–10.26).

Conclusion: The blocking experiments indicate the *H. pylori* specificity of the antibody responses to the 4 biliary tract cancer-associated *H. pylori* proteins. In addition, other *Helicobacter spp.* may be associated with biliary cancer. We are currently further analysing antibody responses to *Helicobacter spp.* in more detail using 14 proteins of *H. bilis* and *H. hepaticus*.

Abstract no.: P16.05

THE INTERPLAY BETWEEN *HELICOBACTER* AND *CAMPYLOBACTER* SPECIES AND OTHER GASTROINTESTINAL MICROBIOTA OF COMMERCIAL BROILER CHICKENS

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Background: Poultry represent an important source of foodborne enteropathogens, in particular thermophilic Campylobacter species. Recent studies have reported enterohepatic Helicobacter species in the microbiota of chickens and on processed chicken meat, suggesting that chickens may serve as a reservoir for these species, and potentially may be transmitted to humans.
Aims: To investigate the composition of the intestinal microbiota of chickens prior to slaughter and to determine the bacterial taxa associated with the absence or carriage of Helicobacter and Campylobacter species.
Methods: The fecal microbiota of 31 market-age broiler chickens (56 days) resident on two neighbouring farms was determined using high-throughput sequencing (HTS) and analysed using PCA, DIVERSE and SIMPER. Species-specific PCR was undertaken to confirm the prevalence and relative abundance of *Helicobacter pullorum* and *Campylobacter concisus*.
Results: Based on HTS the gastrointestinal microbiota of chickens were classified into four potential enterotypes. While variations in farm conditions possibly contributed to microbiota differences, each of the four enterotypes was detected in both farms, suggesting these groupings did not occur by chance. Further differences in the prevalence of *Campylobacter jejuni* subspecies doylei and the emerging species, *C. concisus*, *H. pullorum* and *H. brantae* were observed within these enterotypes. Microbial taxa that potentially could increase the likelihood of colonization by Helicobacter and Campylobacter pathogens were identified.
Conclusion: Depletion of microbial taxa associated with an increase in pathogens and addition of taxa that compete with pathogens, could potentially form the basis of competitive exclusion strategies to eliminate them from the gastrointestinal tract of chickens.

Abstract no.: P16.06

AVAILABILITY OF A SPECIFIC SYNTHETIC ANTIGEN OF *HELICOBACTER HEPATICUS* FOR THE SEROLOGICAL DIAGNOSIS IN HUMAN

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Background & Aim: We developed a monoclonal antibody HRII-51 with high specificity for *H. hepaticus*. MAb HRII-51-immunoreactant was a histone-like DNA binding protein of *H. hepaticus* with molecular weight of 15 kDa (HH-15). Synthesized HH-15 was considered as a useful ligand for serological diagnosis of *H. hepaticus* infection in mice (EHSG 2013). The aim of this study was to examine the availability of synthetic HH-15 for human sera.
Methods: HH-15 antigen was synthesized by Fmoc solid phase chemistry (synthetic antigen HH-15). Direct sandwich ELISA was prepared in which synthetic antigen HH-15 was immobilized on ELISA plates. Serum samples were obtained from 183 patients infected with HCV and 144 healthy subjects. 20 samples were also tested after absorption with *H. hepaticus* cell lysate.
Results: Significant reduction of ELISA value was observed after absorption with *H. hepaticus* cell lysate ($p < 0.01$). Mean ELISA value was 0.589 ± 0.306 in patients with HCV infection and it was higher than that in healthy subjects (0.383 ± 0.141, $p < 0.01$). Level of IgG was not different between the groups. When a cut-off value for *H. hepaticus* seropositivity was defined as the mean OD value plus 2-fold standard deviation of absorbed sera from healthy subjects, positivity of the synthetic antigen HH-15-based ELISA was 33.9% in patients with HCV infection and 4.2% in healthy subjects.
Conclusion: Synthetic histone-like DNA binding protein of *H. hepaticus* would be useful for the diagnosis of *H. hepaticus* infection. Infection of *H. hepaticus* would be more frequent in patients infected with HCV.

Abstract no.: P16.07

META-ANALYSIS OF FIRST-LINE TRIPLE THERAPY FOR *HELICOBACTER PYLORI* ERADICATION IN KOREA: IS IT TIME TO CHANGE?

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Proton pump inhibitor (PPI)-based triple therapy consisting of PPI, amoxicillin, and clarithromycin, is the recommended first-line treatment for *Helicobacter pylori* infection. However, the eradication rate of triple therapy has declined over the past few decades. We analyzed the eradication rate and adverse events of triple therapy to evaluate current practices in Korea. A comprehensive literature search was performed up to August 2013 of 104 relevant studies comprising 42,124 patients. The overall eradication rate was 74.6% (95% confidence interval [CI], 72.1–77.2%) by intention-to-treat analysis and 82.0% (95% CI, 80.8–83.2%) by per-protocol analysis. The eradication rate decreased significantly from 1998 to 2013 ($p < 0.001$ for both intention-to-treat and per-protocol analyses). Adverse events were reported in 41 studies with 8018 subjects with an overall incidence rate of 20.4% (95% CI, 19.6–21.3%). The available data suggest that the effectiveness of standard triple therapy for *H. pylori* eradication has decreased to an unacceptable level. A novel therapeutic strategy is warranted to improve the effectiveness of first-line treatment for *H. pylori* infection in Korea.

Abstract no.: P16.08

COMPARISON OF *HELICOBACTER PYLORI* ERADICATION RATE BETWEEN IATROGENIC AND NON-IATROGENIC GASTRIC ULCER

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Background: Some studies reported that eradication rate of *Helicobacter pylori* (*H. pylori*) in gastric ulcer disease is higher than non-ulcerative gastric disease. Virulence factor and genotypes of *H. pylori* concerning non-iatrogenic gastric ulcer and iatrogenic gastric ulcer is different and may affect eradication rate. Aim of this study was to compare *H. pylori* eradication rate between iatrogenic gastric ulcer and non-iatrogenic gastric ulcer.
Method: Among patients with iatrogenic gastric ulcer from endoscopic removal of tubular adenoma or early gastric cancer or non-iatrogenic gastric ulcer from Jan, 2009 to Dec, 2013 in Yeungnam university hospital, patients diagnosed as *H. pylori* infection and treated were enrolled and reviewed retrospectively.
Results: Among 274 patients enrolled, 166 patients had iatrogenic gastric ulcer and 108, non-iatrogenic gastric ulcer. Mean age (years $\pm$ SD) was 64.5 ± 8.8 in iatrogenic group and 54.7 ± 11.7 in non-iatrogenic group with significant difference ($p < 0.001$). Male proportion and smoking was not significantly different between two groups. *H. pylori* eradication rate was 110/166 (66.3%) in iatrogenic group and 88/108 (81.5%) in non-iatrogenic group with significant difference ($p = 0.006$). By multivariate analysis, only age was associated with difference in *H. pylori* eradication rate.
Conclusion: *H. pylori* eradication rate was significant lower in patients with iatrogenic gastric ulcer following endoscopic removal of adenoma or early gastric cancer than non-iatrogenic gastric ulcer. As eradication of *H. pylori* in iatrogenic gastric ulcer has preventive role, further studies to find ways to raise *H. pylori* eradication rate in old age and iatrogenic gastric ulcer is needed.

P17. Hepatobiliary Diseases

Abstract no.: P17.01

CONCOMITANT INFECTION *HELICOBACTER PYLORI* AND FEATURES COURSE OF HCV-ASSOCIATED CHRONIC LIVER DISEASE

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Aim: Compare the course of chronic HCV-infection in Crimean population patients depending on *H. pylori*-status.
Methods: 95 patients with HCV chronic viral hepatitis (CVH) and 51 patients with HCV liver cirrhosis (LC) are distributed in the study and control groups, depending on the status of *H. pylori*.
Results: Chronic atrophic gastritis met significantly more frequent in *H. pylori*-positive patients with both CVH (26.18% vs 0.00%, $p < 0.05$) and LC (39.13% vs 16.67%, $p < 0.05$).
Noted a higher prevalence of SIBO in *H. pylori* - positive patients with chronic HCV-infection (LC: 73.91% vs 28.89%, $p < 0.05$). In *H. pylori* (+) patients with chronic HCV-infection complicated small intestinal bacterial overgrowth (SIBO) had higher levels of hydrogen (CHC *H. pylori* (+): 27.31 $\pm$ 3.46 ppm, $p < 0.05$, LC *H. pylori* (+): 59.01 $\pm$ 6 18 ppm, $p < 0.05$).
In the *H. pylori* (+) group of patients with LC minimal hepatic encephalopathy was observed significantly more frequently in comparison with the control group (82.35% vs 22.22%, $p < 0.05$).
Conclusions: Analysis of *H. pylori*-positive patients with chronic HCV-infection in the Crimean population, showed a higher prevalence of gastric mucosal atrophy and its close associative relation with SIBO. The relationship in patients with chronic viral hepatitis and the liver cirrhosis (HCV) can be a predictor of an unfavorable course of the disease.

Abstract no.: P17.02

HELICOBACTER PYLORI AND BILE MICROBIOTA IN PATIENTS WITH CHRONIC NONCALCULAR CHOLECYSTITIS

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Aim: To study of presence *H. pylori* and other microbial flora in the bile samples of patients with chronic noncalcular cholecystitis.
Materials and Methods: In this study 210 patients (146- F, 64 - M) with chronic cholecystitis were included. The average age of patients was 43.6 years. Bile samples were separated into three portions: duodenal contents (portion A); gallbladder contents (portion B), bile ducts contents (portion C). Smears prepared from the bile were stained by cationic blue O (basal) and by Gram method.
Results: Microbial association was detected in the duodenum, the gallbladder, the bile ductus accordingly: Gram-positive cocci (staphylococci, streptococci) in 200 (95.2%), 162 (77.1%), 161 (76.7%) cases; Gram-negative rods in 121 (57.6%), 97 (46.2%), 89 (42.4%) cases; *H. pylori* in 178 (84.8%), 87 (41.4%), 133 (63.3%) cases; fusobacteria in 132 (62.9%), 69 (32.9%), 76 (36.2%) cases; actinomyces in 17 (8.1%), 9(4.3%), 6(2.9%) cases; yeast-like fungi of genus Candida in 204 (97.1%), 145 (69.1%), 157 (74.8%) cases; Giardia lamblia in 58 (27.6%), 67 (31.9%), 73 (34.8%) cases; Entamoeba coli in 69 (32.9%), 72 (43.3%), 75 (35.7%) cases. *H. pylori* in the bile had typical morphology (spiral-shaped rod) and was associated with different morphological changes (proliferation, dysplasia, metaplasia) of bile mucosa.
Conclusion: The findings of this study indicate the possible influence of *H. pylori* and other microbial flora (mainly gram-positives cocci, gram-negative rods, yeast-like fungi) on the inflammation of gallbladder mucosa. The received data support the concept of association of *H. pylori* and microbiota with chronic cholecystitis, which requires further researches.

P18 *H. pylori* and Gastric Cancer

Abstract no.: P18.01

SLOW OVERMETHYLATION OF HOUSEKEEPING GENES IN THE BODY MUCOSA IS ASSOCIATED WITH THE RISK FOR GASTRIC CANCER

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Helicobacter pylori (H. pylori) infection increases age-related diverse overmethylation in gene-control regions, which increases the risk of gastric cancer. The *H. pylori*-associated overmethylation changes subsequently disappear when gastric atrophy and cancer develop. To identify cancer-risk epigenotypes, we traced dynamic methylation changes in the background mucosa of the stomach depending on the extent of gastric atrophy. Paired biopsy specimens were obtained from the non-cancerous antrum and body mucosa of 102 cancer patients and 114 *H. pylori*-positive and 112 *H. pylori*-negative controls. The grade of gastric atrophy was evaluated using the endoscopic atrophic border score. The methylation-variable sites at the CpG-island margins and near the transcriptional start sites lacking CpG-islands were semiquantitatively analyzed by radioisotope-labeling methylation-specific PCR. We selected eight housekeeping genes adjacent to Alu (CDH1, ARRDC4, PPARG, and TRAPPC2L) or LTR retroelements (MMP2, CDKN2A, RUNX2, and RUNX3) and eight stomach-specific genes (TFF2, PGC, ATP4B, TFF1, TFF3, GHRL, PGA, and ATP4A). Analysis of age-related methylation in the *H. pylori*-positive controls revealed slow overmethylation in the body and in the LTR-adjacent genes. A high-frequency overmethylation defined based on the slowly overmethylated genes was frequently observed in the body of gastric cancer patients with open-type atrophy (odds ratio, 12.7; 95% confidence interval, 3.2–49.8). The rapidly changing methylation of Alu-adjacent genes was barely increased in the antrum of gastric cancer patients. Among diverse methylation changes associated with *H. pylori* infection, an increase in slowly changing methylation could serve as a cancer-risk marker.

Abstract no.: P18.02

ACTIVE GASTRITIS IN *HELICOBACTER PYLORI* NEGATIVE PATIENTS: A NEW ENTITY?

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Background: Polymorphonuclear cell infiltration (PMN) of the gastric mucosa is predictive for *Helicobacter pylori (H. pylori)* associated gastritis.
Aim: To investigate the prevalence and etiology of PMN in gastritis patients without *H. pylori* infection.
Material and Methods: We enrolled 386 patients (age range 19–94, mean 56y) prospectively, who underwent upper endoscopy in the time period 2011–2014. *H. pylori* status was determined by culture, RUT, histology, *H. pylori* and CagA-serology. Histology was assessed according to the Updated Sydney System. 66 patients with gastric cancer, ulcer and neuroendocrine tumor were excluded for the further analyses.
Results: PMN infiltration was found in 120/320 patients (38%). 109 of 120 PMN positive cases were *H. pylori* positive in at least one of the tests, while 11 patients (3.4% of the total, 9% of the PMN positive population) showed PMN infiltration but were *H. pylori*-negative in *all* tests. Among these 11 patients (Table 1), 4 had histologically proven chronic gastritis and 7 had chronic atrophic gastritis. PMN infiltration was present in at least 2 biopsy sites in 6 patients and was always accompanied by lymphocyte infiltration. Furthermore, 6 patients exhibited corpus predominant atrophy, 5 of them intestinal metaplasia (Table 1).
Conclusion: PMN-Infiltration of gastric mucosa is rare in *H. pylori* negative patients. Although this form of gastritis may represent a new entity, certain known etiologies (such as autoimmune gastritis, toxic damage) could, at least partially, explain the PMN infiltration of the gastric mucosa.

Abstract no.: P18.03

INFLUENCE OF PROSTATE STEM CELL ANTIGEN GENE POLYMORPHISMS AND DUPA GENE STATUS ON SUSCEPTIBILITY TO *HELICOBACTER PYLORI*-ASSOCIATED DISEASES

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Background: Patients with duodenal ulcer (DU) have a reduced risk of developing gastric cancer (GC) compared to those without. Recently, the prostate stem cell antigen (PSCA) rs2294008 C>T polymorphism and *Helicobacter pylori* dupA status were found to be associated with different pathogenesis of DU and GC developments. We examined the influence of the PSCA rs2294008 C>T polymorphism on susceptibility to *H. pylori*-related diseases and the relationships between PSCA polymorphism, dupA status, and gastric mucosal atrophy.
Methods: PSCA rs2294008 C>T polymorphism was assessed in *H. pylori*-positive Japanese patients (n = 488) with non-cardia GC (n = 193), gastric ulcer (GU) (n = 84), DU (n = 61), and atrophic gastritis (n = 150), as well as in *H. pylori*-negatives (n = 266). DupA status was assessed in atrophic gastritis patients. Serum pepsinogen (PG) levels were measured, as a serological marker of gastric mucosal atrophy.
Results: Frequency of PSCA rs2294008 C/C genotype in DU was 36.1%, which was significantly higher than those with GC (12.4%), GU (19.0%), atrophic gastritis (10.7%) and *H. pylori*-negatives (19.5%) ($p < 0.001$). Compared with DU, having the PSCA rs2294008 T allele significantly increased the risk of GC (OR: 3.97, 95% CI: 2.02–7.80; $p < 0.001$), GU (2.40, 1.13–5.10; $p = 0.023$), atrophic gastritis (4.72, 2.26-9.86; $p < 0.001$). Mean PG I/PG II ratio in T allele carriers (2.17 ± 0.75) was significantly lower than that in C/C genotype (3.39 ± 1.27, $p < 0.001$). The dupA status had no effect on progression of gastric atrophy.
Conclusions: The PSCA rs2294008 C>T polymorphism is associated with differing susceptibilities to *H. pylori*-associated diseases. PSCA rs2294008 T allele carriers have increased risk of GC but not DU.

Table 1 Clinicopathological characteristics of PMN positive H. pylori-negative patients

Patient (Nr.)	Age	Gender	Diagnosis	PMN region	Atrophy region	IM	PPI	NSAID	Eradication
164	56	M	Chronic gastritis	Antrum	–	–	–	–	–
204	64	M	Chronic gastritis	Antrum	–	–	Yes	–	–
351	26	M	Chronic gastritis	Antrum, corpus	–	–	Yes	–	Yes
382	50	M	Chronic gastritis	Antrum, corpus	–	Yes	–	Yes	–
38	53	M	chronic atrophic gastritis	antrum, corpus	Antrum	–	–	Yes	–
90	54	M	Chronic atrophic gastritis	Antrum, corpus	Corpus	–	–	–	–
104	41	F	Chronic atrophic gastritis	Corpus	Corpus	Yes	–	Yes	–
106	79	F	Chronic atrophic gastritis	Corpus	Corpus	Yes	Yes	Yes	–
183	77	M	Chronic atrophic gastritis	Antrum, corpus	Antrum, corpus	Yes	–	–	–
210	50	F	Chronic atrophic gastritis	Antrum, corpus	Corpus	Yes	–	–	Yes
249	51	M	Chronic atrophic gastritis	Antrum	Corpus	Yes	–	–	–

Abstract no.: P18.04

cagA STRUCTURAL TYPES AND LONG-TERM SURVIVAL OF PATIENTS GASTRORESECTED FOR CARCINOMA

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Introduction: Infection by cagA positive *H. pylori* strains increases the risk of developing gastric carcinoma. cagA gene may present numerous genomic repetitions in the variable 3′ region, which contains the EPIYA motif where CagA undergoes phosphorylation. This variability may be associated with different clinical outcomes. We examined the variable region of cagA genes of *H. pylori* infected patients who underwent gastroresection for carcinoma.
Patients and Methods: DNA was extracted from gastric mucosa samples of 302 patients and the cagA 3′ region of *H. pylori* was amplified by PCR using primers spanning the entire variable region. The cagA structural types were classified in A (the smallest size), B/D and C (the biggest size) types on the basis of the amplicon dimension. cagA structural types were related to long term survival (20 years) using the Kaplan–Maier method.
Results: One hundred sixty-four patients (54.3%) were cagA positive; 75 patients (45.7%) had organisms with cagA structural type A, 36 (22.0%) type A-B/D, 8 (4.9%) type A-B/D-C, 25 (15.2%) type B/D, 13 (7.9%) type B/D-C and 7 (4.3%) type C strains. Only 17% of patients with type C strains versus 50% with type A survived at 20 years from the operation ($p < 0.001$). Patients with cagA type C strains had distant metastases in 42.9% of cases ($p = 0.004$ vs the other types).
Discussion: Patients operated for gastric carcinoma have the best and the worst prognosis when they are infected by *H. pylori* cagA structural types A and C, respectively.

Abstract no.: P18.05
This abstract has been withdrawn.

Abstract no.: P18.06

CLINICAL CHARACTERISTICS AND OUTCOMES FOR GASTRIC CANCER PATIENTS AGED OVER 80 YEARS: A RETROSPECTIVE CASE-CONTROL STUDY

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Background: The average human life expectancy is increasing, thus proportion of elderly gastric cancer patients are also increasing. However, there have been few reports describing outcomes of elderly gastric cancer in general. Therefore, we investigated clinicopathological characteristics and survival in elderly patients through a case-control study.
Methods: From January 2004 to December 2010, 291 patients aged over 80 years old (case group) were diagnosed with gastric cancer at Asan Medical Center. At same period, 291 patients aged 18 to 80 years old were selected as control group. Clinicopathological findings and outcomes were reviewed retrospectively and compared between the two groups.
Results: The case group showed significant differences in positive family history, presence of symptoms, macroscopically advanced gastric cancer, differentiation, stage, and resectability compared with control group. There was no difference in the rate of *Helicobacter pylori* infection between the two groups. In clinical outcomes, there was a significant difference in overall mortality between the two groups (70.4% vs 26.8%, $p < 0.001$). The distribution of stage according to presence of symptoms showed a trend toward a lower clinical stage in absence of symptoms than presence of symptoms in both of case group and control group. Moreover, there showed a significantly longer overall survival in patients without symptoms than symptomatic patients in case group ($p < 0.001$).
Conclusion: Gastric cancer in elderly patients aged over 81 years showed distinctive clinicopathological features. Although elderly patients showed advanced stage at diagnosis and poor prognosis, early detection in asymptomatic patients, could improve survival outcomes.

Abstract no.: P18.07

INCOMPLETE TYPE OF INTESTINAL METAPLASIA HAS THE HIGHEST RISK TO PROGRESS TO GASTRIC CANCER: RESULTS OF THE SPANISH FOLLOW-UP MULTICENTER STUDY

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Introduction: In high or moderate risk population, surveillance of patients at risk of progression from gastric precursor lesions (PL) to gastric cancer (GC) is recommended. The incomplete type of intestinal metaplasia (IM) may be considered as the best candidate, but more research is needed.
Aims: (i) To evaluate the risk of progression to GC in patients with PL; and (ii) To assess the effect of virulence factors of *H. pylori* infection, the effect of polimorphisms of candidate genes, and the effect of epigenetic variants. Results regarding the first aim are described in this presentation.
Methods: Multicenter follow-up study including 649 patients, diagnosed with PL between 1995 and 2004, in 9 Spanish hospitals, which repeated the endoscopy and biopsy (Sidney protocol) during 2011–2013. Fresh gastric mucosa, saliva sample, and questionnaire on habits of life were collected. DNA from paraffin blocks of recruitment biopsy was used for analysis of *H. pylori* (PCR) and of methylation patterns (Infinium-450-K-methylation-arrays). Based on morphology, IM was sub-classified as complete (small intestinal type, CIM) and incomplete (colonic type,IIM). Analysis was done using Cox-proportional hazards-risk (HR) models.
Results: At baseline, 24% of patients had atrophic gastritis, 38%CIM, 34% IIM, and 4% dysplasia. Mean follow-up was 12 years. 24 patients (3.7%) developed a gastric adenocarcinoma during follow-up. The incidence rate of GC was 2.76 and 5.76 per 1000 person-years, for those with CIM and IIM respectively. The HR of progression to CG was 6.4(95% CI = 0.8–49.6) and 2.4 (0.3–19.8) for those with IIM and CIM at baseline, compared with those with chronic atrophic gastritis.
Conclusion: Patients with IIM have the highest risk of progression to GC.

Abstract no.: P18.08

ASSOCIATION BETWEEN GLYCOGEN SYNTHASE KINASE-3 BETA AND *H. PYLORI* IN DIFFERENT GASTRIC PATHOLOGIES

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Background: Ectopic activation of the Wnt signaling pathway occurs in multiple human cancers. Glycogen synthase kinase-3beta (GSK-3β) regarded as a multifunctional serine/ threonine kinase plays a crucial regulatory role in the Wnt signal transduction pathway. However, the change of GSK-3β and phosphorylation of GSK-3β (the inactive state of GSK-3β) in gastric cancer tissues and their association with *Helicobacter pylori* (*H. pylori*) remain unknown.
Method: We examined expression of GSK-3β and phosphorylation of GSK-3β by immunohistochemical procedure from 165 patients with or without *H. pylori* infection who underwent endoscopy at our hospital.
Results: We found that there was a statistically significant difference on the expression of GSK-3β ($p < 0.001$) and phosphorylated GSK-3β ($p < 0.05$) in various stages of gastric mucosal lesion. In the 79 cases of *H. pylori* positive group, the result was also obvious. Besides expression of them were independent of *H. pylori* infection in chronic gastritis, intestinal metaplasia and atypical hyperplasia group ($p > 0.05$) but not in gastric carcinoma group ($p < 0.05$). And also in the *H. pylori* positive gastric cancer group, the expression of GSK-3β reduced and phosphorylated GSK-3β rose.
Conclusion: Expression of GSK-3β decreases and phosphorylated GSK-3β increases in gastric cancer tissues, especially in *H. pylori* positive patients. The

inactivation of GSK-3β is related to the initiation or progression of gastric cancer. *H. pylori* may be involved in the inactivation of GSK-3β.

Abstract no.: P18.09

HELICOBACTER PYLORI vacA I1/-D1 GENOTYPES COULD BE IMPLICATED AS RISK BIOMARKERS FOR GASTRIC CANCER IN ARDABIL: A VERY HIGH-INCIDENCE AREA OF GASTRIC CARDIA CANCER IN IRAN

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Association between *H. pylori* virulence genes and gastric cancer (GC) has not been reported in Ardabil, a northwestern province of Iran, which is one of the areas with the highest gastric cardia cancer incidence rate in the world (ASRs = $51.8/10^5$ for males and $24.9/10^5$ for females). The present study was aimed to determine the prevalence of *H. pylori vacA* genotypes and investigate whether it could be correlated with risk of GC in Ardabil. Genomic DNA was extracted from gastric tissue of 82 *H. pylori*-infected patients that included 47 gastritis patients (NAG: non-atrophic gastritis) and 35 GC patients. Amplification of *H. pylori 16S rDNA* gene and *vacA* genotypes was performed by PCR. The following genotypic frequency was observed: *vacA m1* (45.23%), *m2* (54.76%), *i1* (53.84%), *i2* (44.61%), *d1* (62.31%), *d2* (37.68%). Statistical analysis showed that frequency of the *vacA i1, d1, m1i1,* and *m1d1* genotypes in patients with GC (76%, 79.4%, 50%, and 48.5%, respectively) was higher than in those with NAG (48.6%, 47.1%, 22.2%, and 18.8%, respectively) ($p < 0.05$). There was a lower prevalence of the *vacA i2, d2, m2i2, m2d2,* and *i2d2* genotypes in GC group (28%, 23.5%, 14.3%, 18.2%, and 18.5%, respectively), compared with in those with NAG group (62.9%, 52.9%, 58.3%, 50%, and 50%, respectively) ($p < 0.05$). The *vacA i-* and *d-* (but not m-) region genotypes were independently associated to GC risk. We have proposed that the *H. pylori vacA d1, i1. m1i1, m1d1* genotypes has increased risk of GC in Ardabil province.

Abstract no.: P18.10

DIFFERENCES IN GASTRIC MICROBIOTA IN GASTRITIS AND GASTRIC CANCER

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We tested the hypothesis that bacteria other than *Helicobacter pylori* exist in the stomach and that an altered gastric microbiota is present in gastric cancer (GC). We studied 25 GC cases and 73 chronic superficial gastritis control subjects. 16S rRNA bacterial genes were amplified in gastric biopsy specimens using primers targeting the V5-V6 regions, sequenced by the Ion PGM sequencing platform, and aligned for taxonomic classification to fully sequenced bacterial genomes using the QIIME pipeline. From the 98 gastric samples, a total of 13.108.150 16S rRNA filtered sequences were obtained. Assessment of the diversity of the gastric microbial community structure showed that GC cases had significantly decreased diversity ($p = 0.01$). The comparison of GC and gastritis cases for the presence and relative abundance of taxa showed that GC cases had an enrichment of the phylum *Proteobacteria* (77% vs 55% relative abundance for GC and gastritis cases, respectively) and depletion of *Bacteroidetes, Firmicutes,* and *Fusobacteria* (3% vs 14%; 10% vs 20%; and 0.1% vs 2%, respectively). Within *Proteobacteria,* the relative enrichment was most noticed for the families *Xanthomonadaceae* (19% vs 0.3%; $p < 0.001$) and *Alcaligenaceae* (16% vs 3% $p < 0.001$).

Our findings that there is an altered stomach bacterial community associated with GC may impact GC prevention and treatment strategies of patients with precancerous disease. These results may provide a new interpretative frame for the incomplete efficacy of successful eradication of *H. pylori* in preventing GC. Further studies are needed to evaluate the clinical impact of these findings.

Abstract no.: P18.11

THE STRATEGY OF TEST AND TREAT FOR *H. PYLORI* INFECTION TO JUNIOR AND SENIOR HIGH SCHOOL STUDENTS IN HOKKAIDO, JAPAN

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Aim: Earlier eradication of *H. pylori* is considered to be more effective for prevention of gastric cancer. The aim of this study is to evaluate the youth's infection rate of *H. pylori* (IR) and to establish the method for test and treat approach for *H. pylori* to junior and senior high school students (test and treat).
Method: We performed test-and-treat in collaboration with local medical association and local government in several areas in Hokkaido.
Results: A total 599 students in three local towns were participated in this study. In yubari city, urine *H. pylori* antibody screening test was conducted to elementary school, junior and senior high school students. The consultation rate (CR) were 62%, 47%, 39%, respectively. The IR was 5.0% (16/317). In Wakkanai city, test and treat was done to high school students, which CR was 62.7% (78/116). The IR was 7.7%, and all *H. pylori* positive students wished eradication therapy and were successful with no severe adverse effects. 204 youths underwent the test (CR = 82.3%) in Fukushima town, and the IR was 7.8% (16/204), the IR was 5.2% (5/96) when limited to the junior high school students. Fifteen of 16 had been treated and eradication rate was 76.9%.
Conclusion: Collaboration of local medical association, local government, and researcher could achieve good consultation rate. The *H. pylori* positive rate of these young generations was relatively low (5-8%), which suggested that it was able to carry out the test-and-treat approach to junior and senior high school students.

Abstract no.: P18.12

IMPACT OF IQGAP1 INHIBITION DURING *HELICOBACTER PYLORI* INFECTION

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The regulation of tight junctions is a key element in the initiation of infection by *Helicobacter pylori* to allow gastric carcinogenesis. IQGAP1 is a scaffold protein which plays a crucial role in cell adhesion and modulates cadherin-based cell adhesion. Our aim was to identify the role of IQGAP1 during *H. pylori* infection and gastric adenocarcinoma development. In a previous work, we have shown that the invalidation of one allele of IQGAP1 gene in mice facilitates the development of gastric pathology and of high grade dysplasia in response to CagA-positive *H. pylori*. The aim of this current study was to identify, *in vitro,* the function of IQGAP1 during the epithelial-to-mesenchymal transition induced by *H. pylori*.

Two different gastric epithelial cell lines were transfected with siRNA targeting IQGAP1. These cells were infected or not with CagA-positive *H. pylori*.

Using western blot and RT-PCR, mesenchymal and epithelial markers expression was quantified. Furthermore, CD44 expression was evaluated by flow cytometry. The ability of the cells to form tumorspheres was tested. The invasion properties of the cells were evaluated using a Transwell assay.

IQGAP1 inhibition induces an increase in mesenchymal markers expression and CD44. Furthermore, the cells transfected with the siRNA show more: (i) hummingbird phenotype, (ii) invasion properties, (iii) ability of forming tumorspheres. Cells transfected and infected do not show a more pronounced mesenchymal phenotype nor more cancer stem cells properties than the transfected and uninfected cells.In conclusion, these results suggest that IQGAP1 destabilization could certainly play an important role in gastric carcinogenesis.

Abstract no.: P18.13

THE GASTRIC CANCER DEVELOPMENT IN PEPTIC ULCER PATIENTS WITH *HELICOBACTER PYLORI* INFECTION

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Background: *Helicobacter pylori* (*H. pylori*) is a risk factor for gastric cancer. We investigate the incidence for gastric cancer development in peptic ulcer patients with *H. pylori* infection.

Method: This was a retrospective study created from chart review for patients who diagnosed by gastric cancer in peptic ulcer patient with *H. pylori* infection between 2003 and 2013. They consisted of 86 gastric ulcer patients and 15 duodenal ulcer patients.

Result: The prevalence rates of gastric cancer in gastric ulcer with *H. pylori* infection were 3.60% (86/2387) and in duodenal ulcer with *H. pylori* infection were 0.84% (15/1775). Kaplan-Meier analysis showed that the incidence of gastric cancer in duodenal ulcer patients was lower than that in gastric ulcer patients, and the prognosis of gastric cancer in duodenal ulcer patients was poorer than that in gastric ulcer patients (log-rank test, $p = 0.191$). In univariate and multivariate analysis, pathologic differentiation, stage and cell type were related to gastric cancer in peptic ulcer patients with *H. pylori* infection ($p < 0.05$).

Conclusion: The prevalence rates of gastric cancer were 3.60% in gastric ulcer with *H. pylori* infection and 0.84% in duodenal ulcer with *H. pylori* infection. In duodenal ulcer patients with *H. pylori* infection, the risk of gastric cancer development was less and the prognosis was poorer than that of gastric ulcer patients with *H. pylori* infection. The incidence of gastric cancer in peptic ulcer patients with *H. pylori* infection were related to pathologic differentiation, stage and cell type.

Abstract no.: P18.14

EVALUATION OF IRON METABOLISM IN PATIENTS WITH GASTRIC CANCER AMONG SUBJECTS WHO WERE DEFINED AS HIGHER RISK BY PEPSINOGEN LEVEL

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Background and Aim: Serum antibody to *H. pylori* and level of pepsinogen (PG) have been used to classify the risk for gastric cancer (GC) known as ABC classification. Gastric mucosal inflammation by *H. pylori* infection has been associated iron metabolism. We examined iron metabolism of patients with GC among subjects who had risk for GC.

Methods: 110 patients (age 50–79) who underwent endoscopic resection for early gastric cancer were studied. Control subjects were 141 adults (age 50–79) who received health survey and diagnosed not to have gastric diseases by barium radiography. Serum antibody to *H. pylori*, level of PGs, iron and ferritin were measured. In ABC classification, subjects were classified into higher risk (group C) when atrophic gastritis was positive (both PG I < 70 ng/mL and PG I/II ratio <3.0). Subjects were classified into group B when *H. pylori* was seropositive without atrophic gastritis.

Results: In group C, level of iron was significantly lower in patients with GC in both males and females (97.7 ± 42.8 and 81.0 ± 28.1 μg/dL) comparing with control subjects (121.9 ± 41.0 and 107.4 ± 35.3; $p < 0.001$). Lower level of iron was also observed in male patients with GC in group B ($p < 0.001$). Level of ferritin was significantly lower in female patients with GC comparing with control patients (50.9 ± 40.7 vs 72.4 ± 55.1 ng/mL) in group C ($p < 0.001$).

Conclusions: In middle-aged and elderly subjects, iron metabolism would be different in patients who developed GC. Measurement of iron would be useful to identify subjects with higher risk even after classified by PG level.

Abstract no.: P18.15

SEROPOSITIVITY TO *HELICOBACTER PYLORI* ANTIGENS IN RELATION TO NON-CARDIA GASTRIC CANCER RISK

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Introduction: Several *Helicobacter pylori* (HP) virulence factors are associated with the presence of more severe disease. The aim of the study was to investigate the association of antibodies against CagA, VacA, GroEL, gGT, HcpC and UreA with the risk of non-cardia gastric cancer.

Methods: Patient sample included individuals with histolopathologicaly proven gastric cancer (n = 128, median of age 67.5, males/females 84/44); control group was represented by consecutive dyspeptic patients coming or upper gastrointestinal endoscopy (n = 146, median of age 61, males/females 55/91) having no evidence of gastric mucosa atrophy, without HP eradication and proton pump inhibitor use during the previous month. Presence of CagA, VacA, GroEL, gGT, HcpC, and UreA antibodies was detected by line immunoassay based test on recombinantly expressed HP proteins (recomLine, Microgen, Germany). Statistical tests: χ^2test, logistic regression.

Results: Antibodies against CagA, VacA, GroEL were significantly more often found among cancer patients compared to the control group (89% vs 65.1%; 21.9% vs 12.3%; 83.6% vs 63%, respectively). Seropositivity against different proteins in relation to risk for gastric cancer is shown in the Table 1.

Table 1 Seropositivity against different HP proteins in relation to risk for gastric cancer

	Odds ratio	95% Confidence interval	*p*-value
CagA	4.371	2.280–8.382	0.001
VacA	1.991	1.042–3.804	0.035
GroEL	2.991	1.681–5.320	0.001
UreA	0.958	0.513–1.790	0.893
HcpC	1.546	0.914–2.614	0.103
gGT	1.204	0.740–1.958	0.454
CagA/VacA/GroEL	5.073	1.8653–13.79	0.001

Conclusions: Seropositivity against CagA, VacA and GroEL was associated with increased risk for non-cardia gastric cancer while individuals with triple positivity showed even fivefold increased risk of gastric cancer.

Abstract no.: P18.16

EFFECT OF *HELICOBACTER PYLORI* ERADICATION ON LONG-TERM SURVIVAL RATES AFTER DISTAL GASTRECTOMY FOR GASTRIC CANCER

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Background and Aims: *Helicobacter pylori* eradication is recommended in patients undergoing gastrectomy for gastric cancer (GC). However, recent studies showed that negative *H. pylori* status was a poor prognostic factor for survival in GC patients who underwent surgery. Our aim was to investigate the effect of *H. pylori* eradication on the long-term outcomes after distal gastrectomy for GC.

Methods: We analyzed survival rates of 190 GC patients who were enrolled to a randomized study that evaluated histologic changes of the remnant stomach. The outcomes measured were overall survival (OS) and recurrence-free survival (RFS).

Results: The median follow-up duration was 8.4 years. In the modified intention-to-treat analysis including patients who received *H. pylori* treatment (n = 87) or placebo (n = 82), 5-year OS rates were 98.9% in the treatment group and 91.5% in the placebo group, and Kaplan-Meier analysis showed no significant difference in OS ($p = 0.335$) between both groups. In a multivariate analysis, there was no difference in OS between both groups (age and sex adjusted hazard ratio [aHR] in the treatment group, 0.68; 95% confidence interval [CI], 0.26 to 1.78; $p = 0.426$). Six patients in the treatment group and

7 in the placebo group had GC recurrences. Thus, *H. pylori* treatment did not also affect RFS after distal gastrectomy with aHR of 0.80 (95% CI, 0.27 to 2.39; $p = 0.688$).
Conclusions: *H. pylori* eradication for GC patients who undergo distal gastrectomy seems not compromise survival rates after the surgery.

Abstract no.: P18.17

CORRELATION OF HEALING TYPE OF LESION AND RECURRENCE IN GASTRIC NEOPLASTIC LESIONS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION

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Background: Endoscopic submucosal dissection (ESD) is common treatment modality for gastric neoplasm, especially early gastric cancer. However, compared to surgical resection, local recurrence can be problem. Although endoscopic examinations were usually carried after an ESD for local recurrence, until now there were no reports about the clinical association about local recurrence and endoscopic healing pattern of lesion. The aim of this study was to investigate on correlation between local recurrences and healing types which can be observed with follow-up endoscopy, as well as factors that related to healing types.
Methods: The patients, who had ESD, were enrolled between April 2010 and January 2012. We performed endoscopy at 1st, 6th, 12th months to investigate the local recurrence. Risk factors of local recurrence were evaluated, focusing on endoscopic healing type. Healing type divided into 3 groups; hypertrophic polypoid, scar and nodular lesion for healing. In addition we evaluated the factors that association with healing type.
Results: 141 patients were analyzed from 293 patients after excluding. Healing types of lesions were 9 hypertrophic polypoids (6.4%), 122 scars (86.5%) and 10 nodular lesions (7.1%). 8 patients were recurred, including 1 hypertrophic polypoid, 2 scars and 5 nodular lesions. Healing type, especially nodular lesion, was statistically significant correlated with recurrence ($p = 0.000$). Significant factor for healing type was not detected.
Conclusion: Although most common healing type was scar, most type of recurrence was nodular lesion. Therefore, we should perform endoscopy with biopsy more carefully, when the lesion has nodular change after ESD.

Abstract no.: P18.18

DOES ERADICATION OF *HELICABACTER PYLORI* AFTER ENDOSCOPIC RESECTION OF EARLY GASTRIC CANCER DECREASE RECURRENCE OF GASTRIC CANCER?

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Background: Eradication of *Helicobacter pylori* in patients' undergone endoscopic resection of early gastric cancer has been recommended by guidelines to decrease incidence of metachronous gastric cancer. The aim of our study was to evaluate effectiveness of *Helicobacter pylori* eradication after endoscopic resection of early gastric cancer in preventing recurrence of gastric cancer.
Method: Patients with result of *Helicobacter pylori* study after endoscopic removal of early gastric cancer from Nov 2005 to Aug 2013 in Yeungnam university hospital were enrolled. Baseline characteristics, follow up period, presence of recurrent disease, status of *Helicobacter pylori* was reviewed retrospectively.
Results: Mean age of the patients was 62.7 ± 9.8 years and 103 (72.5%) patients were male. Mean follow up time was 15.5 ± 18.2 months. Among total 353 patients, 226 (61.4%) had no *Helicobacter pylori* infection. Recurrence was seen in 11 (4.9%) patients with no *Helicobacter pylori* infection and 3 (2.1%) with *Helicobacter pylori* infection. Among patients with *Helicobacter pylori* infection, eradication of *Helicobacter pylori* was done in 69 (48.6%) patients. Recurrence of cancer was seen in 2 (2.9%) patients with *Helicobacter pylori* eradication and 1 (1.4%) with persistent *Helicobacter pylori* infection and recurrence rate was not statistically different between two groups.
Conclusion: Presence and eradication of *Helicobacter pylori* infection in patients who underwent endoscopic removal of EGCA does not seem to affect recurrence of cancer. Further large scaled prospective studies defining relationship between status of *Helicobacter pylori* and cancer recurrence including status of intestinal metaplasia and chronic atrophic gastritis is needed.

Abstract no.: P18.19

FEASIBILITY OF ENDOSCOPIC RESECTION FOR MINUTE SUBMUCOSAL CANCER OF THE STOMACH

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Background: The use of endoscopic submucosal dissection (ESD) for the treatment of minute submucosal (SM) invasive cancer that fulfills the current expanded criteria remains controversial. This study investigated the clinicopathological parameters of patients with sm1 gastric cancers to predict lymph node metastasis (LNM) and evaluate the feasibility of ESD as a curative treatment.
Methods: Data from 278 patients who underwent surgical resection of sm1 gastric cancer between 2006 and 2010 were retrospectively collected and their clinicopathological parameters were analyzed to identify predictive factors of LNM.
Results: Of 278 patients, 28 patients (10.1%) had LNM. Multivariate analysis identified multiple lesions, lymphovascular invasion (LVI), SM invasion depth > 500 μm, undifferentiated histology, and ulceration as factors significantly associated with LNM in patients with sm1 gastric cancer. Additionally, SM invasion width/superficial tumor size ratio > 0.04 demonstrated a significant association with LNM in patients with sm1 gastric cancer falling within the current expanded criteria for ESD. LNM was not identified among 35 patients who met the absence of ulceration, SM invasion depth ≤ 500 μm, and SM invasion width/superficial tumor size ratio ≤ 0.04 besides the current expanded indications.
Conclusions: Endoscopic resection can be performed on patients with minute SM invasive, differentiated cancers of ≤3 cm without LNM on pretreatment examination. In addition, if histological assessment shows the absence of LVI and ulceration, SM invasion depth ≤500 μm, and SM invasion width/superficial tumor size ratio ≤0.04, the patient can be carefully observed without additional treatment.

Abstract no.: P18.20

ETHNIC FEATURES OF ATROPHIC GASTRITIS PREVALENCE AND GASTRIC CANCER INCIDENCE IN MONGOLOIDS OF EASTERN SIBERIA

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Aim: To study prevalence of atrophic gastritis in Mongoloids of Eastern Siberia using determination of serum pepsinogens and to compare data with gastric cancer incidence.
Methods: The screening of atrophic gastritis was performed in Evenkia and Tyva. For the study we selected 527 Evenks (225 males, 302 females) in Evenkia, 466 Tyvins (203 males, 263 females) in Tyva aged over 45 years old by random sampling. In all patients we performed clinical examination and determination of pepsinogen-1, pepsinogen-2 and antibodies to *Helicobacter pylori* in blood serum by immunoassay method using test kits "GastroPanel" ("Biohit", Finland). As a marker of severe atrophy of gastric body mucosa we considered the level of pepsinogen-1 less than 25 μg/L and the ratio pepsinogen-1/pepsinogen-2 less than 3. Data on gastric cancer incidence were collected from the file-data of the regional oncology registries of the involved regions.
Results: The prevalence of *H. pylori* infection among surveyed populations was equally high - about 90.0%. The prevalence of severe gastric body atrophic gastritis and gastric cancer incidence were lower in Evenks in comparison to Tyvins (Table 1). Risk factor for severe atrophic gastritis in Evenks and Tyvins was age older 55 years (OR = 2.52, CI 1.11–5.71, $p = 0.03$ for Evenks; OR = 1.88, CI 1.03–3.43, $p = 0.05$ for Tyvins).
Conclusion: The prevalence of atrophic gastritis was associated with the incidence of gastric cancer in Mongoloids of Eastern Siberia.

Table 1 The prevalence of atrophic gastritis gastric cancer incidence in Eastern Siberia

Population	Atrophic gastritis % (Abs.)	*H. pylori* % (Abs.)	Gastric cancer incidence per 100 000
Evenks, n = 527	5.3% (27)	94.1% (496)	20.2
Tyvins, n = 466	9.4% (44)	93.5% (436)	50.7
OR; CI; *p*	0.52; 0.32–0.85; = 0.01	1.10; 0.66–1.84; = 0.81	0.39; 0.23–0.66; < 0.001

Abstract no.: P18.21

CAGA SEROPOSITIVITY IN RELATION TO GASTRIC CORPUS ATROPHY AND GASTRIC CANCER

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Introduction: Infection with cytotoxin associated gene (cagA) positive *Helicobacter pylori*(HP) strain possibly leads to development of gastric ulcers,gastric atrophy and gastric cancer.The aim of this study was analyze the association of HP and CagA positivity with presence of gastric atrophy and gastric cancer.

Methods: Patient sample included dyspeptic individuals with histolopathologicaly proven any grade gastric corpus atrophy (GCA) (n = 119, median of age-69, males/females-44/75) and patients with histolopathologicaly proven non-cardia gastric cancer (GC) (n = 186, median of age-66, males/females-123/63). Control group was represented by dyspeptic patients with hyperemic gastropathy (HG) at endoscopy and no evidence of GCA or GC (n = 743, median of age-53, males/females-513/230). HP seropositivity was determined using anti-HP IgG (Biohit,Finland) and anti-CagA IgG, IgM and IgA (Vector BEST, Russia). In dubious cases presence of HP infection was evaluated also by rapid urease test and histology. Statistical test used-χ^2; logistic regression.

Results: CagA seropositivity was significantly higher in GCA group compared to the control group: 70% (49/70) versus 45% (332/743); $p = 0.004$.HP seropositivity was significantly higher in (GC) patients compared to control group:76% (141/186) versus 60% (448/743); $p = 0.0001$, but CagA positivity didn't differ significantly between the groups:53% (99/186) versus 45% (332/743); $p = 0.54$. Among GC patients 3% (6/186) were HP negative/CagA seropositive,among GCA patients – 8% (9/70),in control group – 7% (49/743) patients were HP negative/CagA seropositive.In logistic regression analysis presence of GCA was associated with the age>50 years (OR = 2.65; 95% CI:1.68–4.18; $p = 0.0001$) and CagA seropositivity(OR = 1.71; 95% CI:1.14–2.55, $p = 0.004$).Presence of GC was significantly associated with male gender (OR = 4.35; 95% CI:3.1–6.2; $p = 0.001$) and HP seropositvity(OR = 1.58; 95% CI: 1.06–2.35; $p = 0.015$).

Conclusions: CagA seropositivity was independently associated with increased risk of GCA,while showed no association with GC in the present patient sample.It could be explained by loss of infection in some patients due to atrophy,as demonstrated by HP negative/CagA seropositive individuals in all groups of patients.

Abstract no.: P18.22

HOW OFTEN SYNCHRONOUS AND METACHRONOUS LESIONS DEVELOP AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR GASTRIC TUMORS?

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Background and Aim: Endoscopic submucosal dissection (ESD) has become a standard method of treatment for gastric tumors. Metachronous recurrence should be a consideration after ESD has been performed. The aim of this study was to review our experiences in the management of patients with synchronous and metachronous lesions, and to evaluate their incidence and clinicopathologic features.

Patients and Methods: We reviewed 194 patients who underwent ESD for gastric tumors between January 2007 and December 2011. Synchronous lesions were defined as secondary gastric tumors detected within 6 months after the initial ESD. Metachronous tumors were defined as those detected more than 6 months after the initial ESD. We investigated the incidence and clinicopathologic features of synchronous and metachronous tumors after ESD.

Results: In total, 20 patients (10.3%) had synchronous lesions and 19 patients (9.8%) had metachronous lesions. The annual incidence of metachronous tumors after ESD was 2.93%. The median period until discovery after initial ESD was 40.1 months. Female patients developed synchronous and metachronous tumors more frequently than male patients ($p = 0.037$). Patients with *H. pylori* infections developed tumors more frequently than those without ($p = 0.04$). There were no significant differences with respect to the type and differentiation of tumors.

Conclusions: Synchronous and metachronous lesions of gastric tumors were considerably prevalent after ESD. Considering the results of this study, careful endoscopic investigation should be performed after ESD for female patients and those with *H. pylori* infections. However, further large-scale and longer prospective studies are needed.

Abstract no.: P18.23

ENHANCED MIGRATION AND PROLIFERATION IN CD44V9-EXPRESSING CANCER STEM-LIKE CELLS WITH *H. PYLORI* INFECTION

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Background: *Helicobacter pylori*-derived CagA act as oncoprotein. Translocated CagA could be degraded by autophagy in host gastric epithelial cells. However, its autophagic pathway was suppressed in CD44 variant 9(CD44v9)-expressing gastric cancer stem-like cells, resulting in the specific accumulation of CagA in these cells (Cell Host Microbe 12(6):764–77, 2012). We assumed that CD44v9-expressing cells have potential high ability of migration and proliferation by accumulation of CagA. The present study was conducted to investigate the role of specific intracellular accumulation of CagA on migration and proliferation ability in CD44v9-expressing cells.

Method: MKN28 cells were transfected with CD44 standard form (CD44s)- or CD44v9-expression vector. Using Xenograft model, we evaluated the effect of *H. pylori* infection on the tumor growth. Scratch assay was performed by using CD44v9-MKN28 infected with *H. pylori* to study cell migration and cell growth in vitro.

Results: In xenograft model, the tumor volumes of CD44v9-MKN28 infected with *H. pylori* was larger than those of CD44v9-MKN28 at day 21 (mean volume 330.6 mm^3 vs 238.4 mm^3, $p = 0.025$). On the other hand, there was no significant difference between the tumor volumes of CD44s-MKN28 infected with *H. pylori* and those of CD44s-MKN28 at day 21. In scratch assay, the scratched areas of CD44v9-MKN28 infected with *H. pylori* were narrower than those of CD44v-MKN28 (% area filled by cells 33.8% vs 44.8%, $p = 0.001$).

Conclusion: Specific intracellular accumulation of CagA enhances the cell migration and proliferation in CD44v9-expressing cells. Autophagy was important host defense to suppress CagA dependent progression of cancer.

Abstract no.: P18.24

THE COMPLEX ANALYSIS OF CORRELATIONS BETWEEN THE SEVERITY OF *HELICOBACTER PYLORI* (*H. PYLORI*) INFECTION, DENSITY OF MICROVESSELS (DMV) AND EXPRESSIVENESS OF INFLAMMATION BY GASTRIC CANCER (GC)

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The correlations between the degree of *H. pylori* gastric mucosa contamination (GMC), the density of CD4, CD8, CD20, CD68, CD34 (DMV) in GM and tumour were evaluated in 47 patients with GC by immunohistochemistry.

It has been established that the number of lymphoid cells (LCs) with *H. pylori* positive inclusions (HpPI) in GM were correlated with the degree of *H. pylori* GMC ($\gamma = -0.565$, $p = 0.009$) and density of CD20 in tumour ($\rho = -0.437$, $p = 0.047$). The multiple LCs with HpPI were observed more often at a low degree of *H. pylori* GMC, than at high (54.5% and 25% accordingly, $p = 0.06$) and the density of CD20 in tumour was higher in case of single LCs with HpCI, that at multiple (38.3 ± 21.1 and 21.4 ± 12.7 cells on UA accordingly, $p = 0.053$). The correlations between the degree of *H. pylori* GMC, the density of CD4, CD8, CD68 and DMV were not observed.

We believe that the received results connected with the prevalence of coccoid and intracellular forms *H. pylori* in patients with GC (Helicobacter, 2012, no. 4, P.113). The absence of correlations between the severity *H. pylori* infection, activity angiogenesis and inflammations testifies that the decrease of 3-years relapse-free survival in patients with high degree of *H. pylori* GMC (Helicobacter, 2013, V.18, P.154) can be associated with the genotoxic effect of *H. pylori*. The negative correlations between degree of *H. pylori* GMC and the number of intracellular forms of bacteria can be connected just as with the presence of two different competing forms *H. pylori* so with the persistence of bacteria in immune cells (for example at presence antibacterial therapy).

Abstract no.: P18.25

GASTRIC FUNCTION ASSESSED BY GASTROPANEL ® IN VERY OLD PATIENTS (OVER 80 YEARS OLD) AND APPROPRIATENESS OF PPIS ADMINISTRATION

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Chronic atrophic gastritis (CAG) is a stomach precancerous condition often related with *Helicobacter pylori* (Hp) infection. Gastropanel® is a non-invasive test able to detect both CAG and Hp infection. In literature no data are available on CAG and the use of PPIs in very old patients.

Aim: To investigate morpho-functional status of gastric mucosa by non-invasive test and the use of PPIs in very old patients.

Materials and Methods: 89 patients (M:F = 1:3) over 80 years old (mean age: 86.98 years old; range: 80–103) consecutively admitted to Internal Medicine and Critical Subacute Care Unit were enrolled in this study. Gastropanel ® was performed in every patients (Biohit®, Helsinki, Finland).

Results: CAG was diagnosed by serology in 42 out of 89 patients (47.2%) namely 17 patients had chronic atrophic body gastritis (Pepsinogen I 10 pmol/L), 20 patients had chronic atrophic antral gastritis (Gastrin 17 < 2 pmol/L under PPIs administration) and 5 patients had atrophic pangastritis (Pepsinogen I < 25 μg/L and Gastrin 17 < 2 pmol/L). Hp infection was present in 44 patients (49.4%). 76 patients had PPI therapy of whom 22 showed a picture of body CAG (N = 17) or chronic atrophic pangastritis (N = 5).

Conclusions: According with epidemiological trends, a picture of CAG was find in 47.2% out of very old patients. In particular, 25.5% of them experienced hypo-achloridria, therefore PPI administration in such patients seems completely inappropriate. Gastropanel® seems to be useful as non-invasive test in critical subjects over 80 y.o in order to assess both gastric morphological and functional disorders.

Abstract no.: P18.26

CHARACTERIZATION OF *HELICOBACTER PYLORI CAGA* AND *VACA* GENOTYPES IN MACAU, CHINA

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Background and Aim: *Helicobacter pylori* virulence factors have been associated with the clinical outcome of the infection. The aim of this study was to evaluate the relationship between *H. pylori cagA* and *vacA* genotypes and gastric carcinoma in Chinese patients living in Macau, China.

Methods: Paraffin-embedded gastric biopsies from 290 patients with chronic gastritis (n = 238) and gastric carcinoma (n = 52) were characterized for *H. pylori cagA* and *vacA* s-, i-, and m- region genotypes by PCR-based techniques.

Results: Of the 281 *H. pylori*-infected patients, 246 (87.5%) were infected with *cagA*-positive strains, with no significant differences between chronic gastritis and gastric carcinoma patients (88.9% vs 80.9%, respectively; $p = 0.146$). Genotyping of *vacA* s-, m-, and i-regions revealed infection with multiple strains in 97 (34.5%) samples, with no significant differences between chronic gastritis and gastric carcinoma patients (36.3% vs 25.5%, respectively; $p = 0.180$). Excluding multiple infections, the prevalence of the high-risk s1, i1, and m1 genotypes was 91.2%, 85.2%, and 52.6%, which was not significantly different between chronic gastritis and gastric carcinoma patients (91.7% vs 88.4%, 85.1% vs 85.3%, and 53.7% vs 47.2%, respectively). *H. pylori* strains of the s1/i1/m1 genotype were present in 43.7% chronic gastritis and in 32.1% gastric carcinoma patients, which was not significantly different.

Conclusion: No relationships between *H. pylori cagA* and *vacA* genotypes and gastric carcinoma were observed, possibly due to the high prevalence of the most virulent genotypes in this population. There is a high prevalence of patients infected with multiple *H. pylori* strains.

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Abstract no.: P18.27

STUDY OF RELATIONSHIP BETWEEN PEPSINOGEN VALUE AND *H. PYLORI* INFECTION

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Background: It is reported that combination of pepsinogen (PG) method (PGI value <70 and PGI/II ratio<3) is useful for detection of high risk group of gastric cancer. In this study, we investigated the relationship between *H. pylori* infection, histological active gastritis and serum PG value.

Methods: The subjects were 349 patients who underwent serological PG & *H. pylori* antibody test and endoscopy. We conducted take biopsy sample for histological evaluation and *H. pylori* infection. We divided 4 group: A; PG method (−) & IgG HP antibody (−), group: B; PG method (−) & IgG HP antibody (+), group: C; PG method (+) & IgG HP antibody (+), group: D; PG method (+) & IgG HP antibody (−). We evaluated histological inflammation, activity, atrophy, intestinal metaplasia and *H. pylori*.

Result: There were 1 (group A), 6 (group B), 20 (group C) and 5 (group D) of gastric cancer. With reference to *H. pylori* infection sensitivity/specificity were PGI:61.1/14.2 (cut off 60), PGII:86.9/85.7 (cut off 11) and PGI/II ratio: 90.3/67.9 (cut off 4.5) respectively. With reference to histological activity sensitivity/specificity was PGI: 46.1/25 (cut off 50), PGII:82.9/71.4 (cut off 13) and PGI/II ratio: 77.1/51.7 (cut off 3.5) respectively.

Conclusion: PG method is useful for detection of high risk group of gastric cancer. On the other hand, serum PG value (especially PGII) is useful for *H. pylori* infection and histological activity.

Abstract no.: P18.28

GASTRIC MICROBIOTA COMPOSITION AND CLINICAL OUTCOME OF *HELICOBACTER PYLORI* INFECTION

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The prevalence of *Helicobacter pylori* infection is higher in developing countries than in the industrialised world, reflecting the critical influence of socioeconomic factors. The prevalence among middle-aged adults is over 80 percent in many developing countries, as compared with 20 to 50 percent in industrialized countries. The outcome of infection with *H. pylori* varies widely, a large fraction of infected individuals remain asymptomatic, a small fraction develop peptic or duodenal ulcers, an even smaller fraction develop gastric adenocarcinoma and MALT-lymphoma. We are investigating whether there is any correlation between the composition of the gastric microbiota and clinical outcome of *H. pylori* infection in the Indian population.

Gastric endoscopy samples were collected from individuals with different clinical symptoms ranging from asymptomatic to peptic and duodenal ulcers to gastric adenocarcinoma and MALT-lymphoma. For each sample 16SrDNA libraries were created using universal primers and next generation sequencing was performed. The relative abundance of different genera in the gastric microbiome of individuals with different clinical symptoms and asymptomatic individuals was compared. In general, the most abundant genera in the gastric microbiota of asymptomatic individuals without *H. pylori* infection or very low abundance of *H. pylori* (less than 1% of the gastric microbiota) were Hemophilus, Streptococcus and Neisseria. None of these genera were detected in patients with high abundance of *H. pylori* and severe gastric lesions, instead a more diverse microbiota with almost equal abundance of Pseudomonas, Flavobacterium, Corynebacterium and Rothia was observed in these samples. The relevance of these observations will be discussed.

Abstract no.: P18.29

RISK FACTORS OF LOCAL RECURRENCE IN PATIENTS WITH TUMOR-POSITIVE LATERAL RESECTION MARGINS AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER

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Background: Because local recurrence occurs frequently in LM+ cases, it is very important how to deal with these cases. The aim of this study was to clarify the clinicopathologic factors related to tumor recurrence in LM+ cases after ESD for EGC.
Methods: From January 2005 to December 2012, a total of 1,083 patients with EGC were treated by ESD at our hospital. Of them, lesions with pathological diagnosis of LM+ were included in this study.
Results: A total of 55 LM+ cases after ESD for EGC were enrolled. Of them, local recurrence was found in 20 (36.4%) during the followed-up period of median 23 months. Incorrect delineation of a lesion extended pathologically beyond ESD marking dots was a main cause of LM+ in 39 (70.9%) cases; in the remaining 16 (29.1%), LM+ was caused by technical ESD-related problems such as the inadvertent intralesional incisions (n = 2) and piecemeal resections (n = 14). In multivariate analysis, the tumor size > 2 cm ($p = 0.027$) and the LM+ length > 6 mm ($p = 0.035$) were the independent risk factors for tumor recurrence.
Conclusion: For decreasing LM+, it is very important to accurately delineate the lateral margins during ESD, and when the final histopathologic result is LM+, the cases with LM+ length > 6 mm or tumor size > 2 cm should be considered for additional surgical resection or re-ESD due to a high risk of tumor recurrence.

Abstract no.: P18.30

IS ENDOSCOPIC SUBMUCOSAL DISSECTION SAFE FOR PAPILLARY ADENOCARCINOMA OF STOMACH?

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Background: Papillary adenocarcinoma of the stomach is known to be associated with higher frequency of lymph node (LN) metastasis, liver metastasis and poorer surgical outcome, compared to tubular adenocarcinoma.
Objective: To investigate the clinicopathologic characteristics and predictive factors for LN metastasis in early gastric cancers (EGCs) with papillary adenocarcinoma, and then to evaluate outcomes of ESD in them.
Design: A retrospective, single-center study.
Patients: From January 2005 to May 2013, 49 patients who underwent surgical operation for EGC with papillary carcinoma were enrolled in group 1, and 24 patients who underwent endoscopic submucosal dissection (ESD) for EGC with papillary carcinoma were in group 2.
Results: EGCs with papillary adenocarcinoma showed predilection to location in the lower one-third of the stomach and elevated shape macroscopically. Overall prevalence of LN metastasis was 18.3% (9/49), and only presence of lymphovascular invasion was associated for LN metastasis ($p = 0.016$). When 49 patients having EGC with papillary adenocarcinoma were applied to current criteria of ESD, 6 were in absolute indication for ESD and 11 were in expanded indication for ESD. Among 17 patients in ESD indication, 2 (11.8%) had LN metastasis. Of 24 patients who underwent ESD, 13 (54%) were in out-of ESD indication; of them, 9 patients underwent surgical operation due to noncurative resection.
Conclustions: Even if EGCs with papillary adenocarcinoma are suspected to belong in ESD indication after pre-treatment work-up, ESD should be considered more carefully because of more frequent LN metastasis and more need for additional surgical operation.

Abstract no.: P18.31

EFFECT OF URTICA DIOICA EXTRACT, MENTHA SPICATA ESSENTIAL OIL AND *MATRICARIA CHAMOMILLA* ESSENTIAL OIL ON *HELICOBACTER PYLORI* IN VITRO

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Helicobacter pylori is the part of natural of the human gastrointestinal on stomach and a common complication for human beings which effect approximately 30% of children and 60% of adults and this phenomenon leads to some disease such as Gastritis, Peptic Ulcers and Stomach cancer. In 70% of cases has neither clues nor significant effects. About half of the people who suffers from the Helicobacter disease; 10–20% leads to gastric ulcer and gastric cancer and in 1–2% of cases leads to Stomach cancer.The use of Antibiotics is the main treatment for this disease but due to the length of treatment and because of the side effects of using the Antibiotics and also as in 20% cases the body of patient resist against Antibiotics; it seems there must be an alternative treatment. The use of Medical plants (Herb) is the best way for the control and treatment of disease.
In regards of the strong and definite anti-bacterial activities of Urtica dioica, and also due to the positive effects of mentha spicata and Chamomile on the gastrointestinal and Ulcers disease in traditional Medicine, the extract of ethanol Mentha spicata, Chamomile essential oil and Mentha spicata essential oil were produced in 2 dilutions and then the inhibitory effects on the development of *H. pylori* was investigated by the disc diffusion method and Agar well diffusion method.The results shown the prevention effects on growth of *H. pylori* up to 50 mm zone diameter for Urtica dioica, 62 mm for Mentha spicata and 57 mm for Chamomile.