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Helicobacter WILEY

# European Helicobacter and Microbiota Study Group

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## Accepted Abstracts

## The European Helicobacter and Microbiota Study Group



**Table of contents**:

| | |
|---|---|
| Workshop W1 Diagnosis and Epidemiology | 3 |
| Workshop W2 *H. pylori* pathogenesis | 6 |
| Workshop W3 Treatment of Helicobacter infection I | 9 |
| Workshop W4 Gastric Carcinogenesis | 14 |
| Workshop W5 Treatment of Helicobacter infection II | 18 |
| Workshop W6 Microbiota in health and disease | 20 |
| Poster Round 1.1: Treatment of Helicobacter infection | 24 |
| Poster Round 1.2 Drug Resistance and clinical issues | 49 |
| Poster Round 2.1 Helicobacter and extragastroduodenal disease | 57 |
| Poster Round 2.2 Gastric microbiota | 61 |
| Poster Round 3.1 Gut microbiota in health and disease | 65 |
| Poster Round 4.1 Diagnosis of Helicobacter infection | 80 |
| Poster Round 4.2 Epidemiology | 87 |
| Poster Round 4.2 Paediatrics | 95 |
| Poster Round 5.1 Gastric cancer and cancerogenesis | 99 |
| Poster Round 6.1 Virulence factors and pathogenesis of Helicobacter infection | 113 |
| Poster Round 6.2 Inflammation, immunity, vaccines and host interaction | 121 |
| Poster Round 6.3 Microbiology and genomics of Helicobacter | 126 |

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Contributions of up to EUR 10.000.- (or equivalent value in kind) per year per entity are considered “Modest”. Contributions above EUR 10.000.- per year are considered “Significant”.

# ABSTRACTS

## WORKSHOP W1 DIAGNOSIS AND EPIDEMIOLOGY

### W1.1 | Apparent intracellular *Helicobacter pylori* detected by immunohistochemistry - the missing link in eradication failure

A. Beer[1]; H. Hudler[2]; M. Kundi[1]; S. Hudler[2]; M. Hader[3]; V. Taeuber[1]; H. Schachner[1]; S. Gruber[2]; A. M. Hirschl[1]; R. Kain[1]; **A. Makristathis**[1]

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**Objective**: *Helicobacter (H.) pylori* is primarily an extracellularly living bacterium. However, intracellular occurrence can often be simulated by immunohistochemical stains. Considering antimicrobial resistance, we investigated the impact of the apparent intracellular *H. pylori* (aiHp) on treatment failure of first-line triple therapies.

**Design**: Gastric biopsies of 814 *H. pylori* infected patients naïve for treatment were analyzed before and after eradication therapy by immunohistochemistry. Thereof, 373 received treatment consisting of amoxicillin, clarithromycin and PPI (AC/PPI). Availability of PCR-based clarithromycin susceptibility test results from pre-treatment corpus biopsies was a pre-condition for matching 52 aiHp to 52 non-aiHp cases within the AC/PPI-group.

**Results**: AiHp were associated with low counts of mostly coccoid forms and were considerably more prevalent in corpus than antrum biopsies (95.2% vs 24.6%); they were found in 497/814 patients (61%) and in 192/373 patients (51.5%) in the AC/PPI-group. The eradication rate in aiHp vs non-aiHp cases was 34.4% vs 72.9% in the entire sample and 45.3% vs 66.8% in the AC/PPI-group. Among the 104 paired patients, respective values were 46.2% vs 78.8%; in clarithromycin susceptible cases 57.1% vs 89.5%. Both aiHp and resistance to clarithromycin proved to be highly significant ($P \leq 0.001$) and independent predictors of eradication failure. Twelve of 13 aiHp cases with a clarithromycin sensitive strain, who failed eradication, developed resistance to the antibiotic.

**Conclusions:** Patients with aiHp are at risk for failure of first-line triple therapy. Immunohistochemical staining for *H. pylori* in corpus biopsies is of importance; occurrence of aiHp should be considered with regard to therapy options.

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### W1.2 | Impact of implementing a real-time PCR assay on the workflow and laboratory diagnosis of *Helicobacter pylori* infection from gastric biopsies

**T. Huang**; P. Bogaerts; M. Hoebeke; W. Bouchahrouf; C. Berhin; Y. Glupczynski

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**Background**: Antimicrobial susceptibility testing (AST) of *Helicobacter pylori* (HP) is crucial for tailored-based treatment regimens. Since culture-based methods are cumbersome, we evaluated the usefulness of a commercial real-time PCR assay to detect HP and clarithromycin resistance in gastric biopsies.

**Methods**: All consecutive gastric biopsies referred from five gastro-endoscopic clinics were tested by Amplidiag®*H. pylori* +ClariR PCR assay (Mobidiag) in batch three times per week. PCR HP-negative and HP-positive clarithromycin-susceptible (CLA-S) results were reported without additional analysis, while culture-based AST (E-test) was performed for HP-positive clarithromycin-resistant (CLA-R) samples. The rates of HP detection with CLA-R rates and the turn-around time (TAT; time from sample reception to results reporting) obtained with this algorithm (May to December 2018; P2) were compared to those obtained during the reference period (January to April 2018; P1) using daily standard culture.

**Results**: An average of 19.8% and 22.3% of the 1448 (P1 by culture) and 2729 (P2 by PCR) processed biopsies were positive for HP with 25.9% and 28.4% of CLA-R found during the periods P1 and P2, respectively. The median TAT for HP-negative and HP-positive CLA-S samples was shortened from 10 days during P1 to 2 days during P2. In total, the number of cultures and of AST processed were reduced by 75%.

**Conclusions**: The implementation of a real-time PCR assay for the detection of HP and clarithromycin resistance status from gastric biopsies resulted in major savings in cultures and marked shortening of TAT, while providing useful information for the selection of appropriate eradication regimens.

T. Huang: None. P. Bogaerts: None. M. Hoebeke: None. W. Bouchahrouf: None. C. Berhin: None. Y. Glupczynski: None.

## W1.3 | Impaired sensitivity of invasive tests for *Helicobacter pylori* infection in patients with severe chronic atrophic gastritis

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**Introduction**: Current guidelines recommend one invasive test during endoscopy as sufficient for confirmation of *Hp* infection. Loss of parietal cells due to chronic atrophic gastritis with consecutive increase of pH values decreases *Hp* density. Reduced *Hp* colonisation may negatively affect sensitivity of all diagnostic tests for *Hp* infection except for serology.

**Aim**: To assess the diagnostic sensitivity of invasive *Hp* tests during the progression of chronic active gastritis to atrophic gastritis with/without intestinal metaplasia assessed by the OLGA/OLGIM staging system.

**Material and Methods**: Data from the prospective ERA-NET cohort was analyzed to investigate diagnostic sensitivity of clinical tests for culture, histology and rapid urea test (RUT) in 197 patients with positive Anti- *Hp* IgG antibodies. Active *H.p.* infection was defined by at least one positive invasive test. After stratification of patients into OLGA 0-1, OLGA 2-4, OLGIM 0-1 and OLGIM 2-4, sensitivity was calculated for each test alone or in combination.

**Results**: Criteria for active *H.p.* infection was fulfilled in 136/197 (69%) patients and comparable between the 4 groups. Sensitivity for histology and RUT fell below 80% in OLGIM/OLGA 2-4.

| | Serology & ≥1 test pos. (reference) | Sensitivity for 1 test positive, n/N, % | | | Sensitivity for 2 tests positive, n/N, % | | |
|---|---|---|---|---|---|---|---|
| | n/N % | Culture | Histology | RUT | Culture & Histology | Culture & RUT | Histology & RUT |
| OLGIM 0-1 | 117/168 69.6% | 107/117 91.5% | 100/117 85.5% | 99/117 84.6% | 112/117 95.7% | 116/117 99.1% | 112/117 95.7% |
| OLGIM 2-4 | 19/29 65.5% | 17/19 89.5% | 15/19 78.9% | 15/19 78.9% | 19/19 100% | 18/19 94.7% | 17/19 89.5% |
| OLGA 0-1 | 97/138 70.3% | 90/97 92.8% | 85/97 87.6% | 85/97 87.3% | 94/97 96.9% | 96/97 96.9% | 93/97 95.9% |
| OLGA 2-4 | 39/59 66.1% | 34/39 87.2% | 30/39 76.9% | 29/39 74.4% | 37/39 94.9% | 38/39 94.8% | 36/39 92.1% |

**Conclusion**: In patients with advanced stages of chronic gastritis with gastric atrophy or intestinal metaplasia sensitivity particularly for histology and RUT decreases. We suggest performing at least two invasive tests for *Hp* in patients with endoscopic findings suggestive of advanced atrophy or intestinal metaplasia.

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## W1.4 | Performance of multiplex serology in discriminating active versus past *Helicobacter pylori* infection

**J. Butt**[1,2]; W. J. Blot[3]; M. J. Shrubsole[4]; M. G. Varga[5]; L. Hendrix[6]; S. Crankshaw[1]; T. Waterboer[2]; M. Pawlita[2]; M. Epplein[1]

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**Purpose**: To feasibly analyze associations of *Helicobacter pylori* (*H. pylori*) with disease in large cohort studies, assays are needed to assess *H. pylori* prevalence in existing biospecimens. However, serology has traditionally been unable to distinguish active from past infection. We sought to determine the sensitivity of sero-positivity to *H. pylori* proteins to detect active infection.

**Methods**: We measured antibody responses to 13 *H. pylori* proteins using multiplex serology in serum samples of a test (n = 78) and validation set (n = 49) collected concurrently from patients undergoing urea breath test (UBT). To determine sensitivity and positive predictive value (PPV) of sero-positivity to *H. pylori* proteins for active infection, a cut-off was applied to achieve 90% specificity. Antibody levels were retested in a subset of participants (n = 9) 6 months after *H. pylori* eradication.

**Results**: With a specificity of 91%, sero-positivity to four (VacA, GroEl, HcpC, HP1564) *H. pylori* proteins ascertained active infection from 100% sensitivity (VacA) to 75% sensitivity (HP1564). The resulting PPVs ranged between 80% (VacA) and 75% (HP1564). The validation set replicated results obtained in the test set. Among those successfully eradicated, antibody levels decreased significantly for three of the four top antigen hits (VacA, HcpC, HP1564) 6 months after baseline assessment.

**Conclusion**: Utilizing the cut-offs for sero-positivity established through comparison with UBT, antibody responses to *H. pylori* proteins VacA, GroEl, HcpC, and HP1564 determine active *H. pylori* infection at high specificity and sensitivity and may approximate the prevalence of active *H. pylori* infection in large cohorts.

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## W1.5 | Racial differences in *Helicobacter pylori* antibody prevalence by year of birth and demographic factors in a consortium of US adults

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**Introduction**: Infection with *Helicobacter pylori* is the greatest risk factor for gastric cancer. Although *H. pylori* infection has been decreasing in the US, there remains a substantial racial disparity in *H. pylori* prevalence. Therefore, we sought to assess *H. pylori* prevalence over time by race and to identify other factors associated with *H. pylori* prevalence in the US.

**Methods**: We utilized multiplex serology to quantify antibody responses to 13 *H. pylori* antigens in 4,476 participants across 5 cohorts. We applied logistic regression to calculate odds ratios (ORs) and 95% confidence intervals (CIs) to determine the association between *H. pylori* sero-prevalence and year of birth and other participant demographic and medical history characteristics.

**Results**: African Americans were more than twice as likely to be *H. pylori* sero-positive as whites (71.3% vs 33.0%). After adjusting for sex, education, case-control status and age, *H. pylori* prevalence remained flat with later birth year (from 1918 to 1966) in African Americans, but significantly decreased among whites ($P_{trend}$<0.0001). For both races, lower levels of education were associated with increased prevalence of *H. pylori* ($P_{trend}$<0.0001). Among whites only, self-reported history of ulcer (OR, 1.58; 95% CI, 1.20-2.08) was associated with *H. pylori* sero-positivity, whereas age, BMI, smoking status, and self-reported history of diabetes were not associated with *H. pylori* status.

**Conclusion**: Our data suggest that *H. pylori* prevalence has significantly declined among whites in the US born from the 1920s to 1960s; however, it has remained stable among African Americans over the same time period.

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## W1.6 | Seroprevalence and determinants of *Helicobacter pylori* infection in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL)

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**Background**: *Helicobacter pylori* infection is the primary known risk factor for gastric cancer. Despite the global decline in *H. pylori* prevalence, this bacterial infection remains a public health concern in developing areas, including Latin America. Since Hispanics/Latinos account for a rapidly growing population in the United States (U.S.), there is a need to monitor and better understand *H. pylori* prevalence and its determinants in this population.

**Methods**: Our cross-sectional study included 16,144 U.S. resident adults (mean age 41 years, 48% males, 23% U.S.-born) from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL), including population groups with contrasting gastric cancer risk. Anti-*H. pylori* antibodies were measured by ELISA using plasma collected in 2008-2011. We used sample weighted logistic regression to calculate odds ratios for associations between *H. pylori* seroprevalence and various socioeconomic and lifestyle factors. We calculated predictive margins from multivariable models.

**Results**: The overall weighted *H. pylori* seroprevalence was 57% among HCHS/SOL participants. Age-adjusted prevalence varied by Hispanic/Latino background, ranging from 47% in Puerto Ricans to 72% in Central Americans. In multivariable-adjusted models, higher age, male sex, lower education level, non-U.S. born status, non-English preference, lower acculturation levels, smoking, high number of missing teeth, and fewer number of doctor visits were each associated (*P*-values < 0.05) with higher *H. pylori* seroprevalence.

**Conclusions**: *H. pylori* seroprevalence in Hispanics/Latinos remains high and differed significantly by Hispanic/Latino background. *H. pylori* seropositivity is strongly associated with poor socioeconomic

conditions and lower acculturation. These findings highlight the ongoing importance of this infection in the U.S.

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## W1.7 | Decreased pepsinogen level in relation to presence of menopause in the GISTAR study population in Latvia

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**Introduction**: Studies suggest that female hormones reduce the risk of gastric atrophy and subsequently gastric cancer.

**Objective**: To analyze decreased Pepsinogen (Pg) level in relation to menopause.

**Material and methods**: Women aged 40-64 years from the GISTAR study in Latvia who completed a questionnaire, were tested for PgI, PgII by latex-agglutination test (Eiken Chemical, Japan) and *Helicobacter pylori (H. pylori)* IgG antibodies (Biohit, Finland). Presence and age at onset of menopause (<50 or ≥50 years), current/previous hormonal replacement therapy (HRT) was compared between women with and without decreased Pg (PgI/PgII ≤ 3 and PgI ≤ 70 ng/mL). A multivariate logistic regression was built for decreased Pg and menopause, adjusting for current/previous HRT, age (≤50 or > 50), level of education, income, smoking, *H. pylori*.

**Results**: A total of 911 women(mean age 51.9, SD ± 6.8 years) were included. Menopause was reported by 54.0%; current HRT-by 4.3%. Decreased Pg level was detected in 301 women and was observed more often in women with menopause compared to women without menopause (35.6% vs 30.1% respectively, $P$ = 0.08). Women currently on HRT were less likely to have decreased Pg (17.9% vs 33.6% respectively, $P$ = 0.04). In multivariate analysis decreased Pg was no longer associated with menopause (OR = 1.1; 95%CI 0.7-1.7; $P$ = 0.6), inversely associated with current HRT (OR = 0.5;95%CI 0.2-1.1; $P$ = 0.09), but had strong association with *H. pylori* (OR = 2.8;95%CI 2.0-3.9; $P$ < 0.001) and age >50 (OR = 1.7;95%CI 1.3-2.3; $P$ = 0.001).

**Conclusions**: Our findings suggest that menopause *per se* is not associated with decreased pepsinogen, however protective effect of HRT against gastric atrophy should be studied more detailed among women on HRT.

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# WORKSHOP W2 *H. PYLORI* PATHOGENESIS

## W2.1 | R-Spondin 3 links gastric epithelial stem cell regeneration to antimicrobial defense against *Helicobacter pylori*

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*Helicobacter pylori* chronically colonize the stomach. A subpopulation of bacteria can colonize the stem cell compartment in the base of the gastric gland.

These bacteria trigger an expansion of the stem cell compartment. We have previously shown that this is driven by Wnt signaling stimulated by R-spondin (Rspo). Infection with *Helicobacter pylori* stimulates increased secretion of Rspo3 by myofibroblasts, leading to increased proliferation of Wnt-responsive Axin2+/Lgr5- stem cells and finally gastric gland hyperplasia. While Axin2+/Lgr5- cells increase their proliferation, the neighboring Lgr5+ do not show increased proliferation upon exposure to Rspo3 and it is not clear how Rspo3 affects these cells. Here we demonstrate that in contrast to its known mitogenic activity, Rspo3 induces differentiation of the basal Lgr5+ cells towards secretory cells. Using 3D organoids we demonstrate that the effect of Rspo3 is concentration dependent: while moderate concentrations induce proliferation, high concentrations inhibit proliferation and instead drive differentiation towards gland base secretory cells. Using single cell RNAseq we characterize this population of Lgr5+ secretory cells and demonstrate that they expand upon infection. We find that upon infection, secretory Lgr5+ cells express antimicrobial factors, such as intelectin1 that are secreted into the lumen to bind, agglutinate and immobilize *H. pylori*. Depletion of Lgr5+ cells or knockout of Rspo3 in myofibroblasts leads to hyper-colonization of gland stem cells with *H. pylori*. In contrast, systemic administration or overexpression of Rspo3 in the stroma clears *H. pylori* from the glands. Thus, the Rspo3-Lgr5 axis simultaneously regulates both antimicrobial defense and mucosal regeneration.

M. Sigal: None. T. Meyer: None.

## W2.2 | *Helicobacter pylori* CagA induces intestinal metaplasia in normal human gastric epithelial cells

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We have employed our human epithelial organoid model (Schlaermann et al. 2014) to introduce and stably express *H. pylori cagA*. Interestingly, CagA protein produced by epithelial cells led to a truncated form of CagA, as previously observed in other human cells for CagA delivered by the type 4 secretion system (T4SS). The processed C-terminal part of CagA was properly phosphorylated by the host cells. CagA-transformed cells displayed a less polarized phenotype compared to mock-transfected organoids, and exhibited a markedly altered gene expression profile. To our surprise, almost all relevant markers characteristic of gastric intestinal metaplasia were induced, while typical gastric markers were downregulated. We further present a histological analysis of cagA-transduced organoids and provide information on the functional significance of the EPIYA phosphorylation sites in CagA as well as the signaling routes involved in the CagA dependent development of gastric intestinal metaplasia.

**References**: Schlaermann, P. et al. 2014. A novel human gastric primary cell culture system for modelling *Helicobacter pylori* infection in vitro. Gut 65, 202-213.

T. Meyer: None. M. Reines: None.

## W2.3 | Inhibition of Autophagy aggravates DNA damage response via Rad51 ubiquitination in response to *H. pylori* infection

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**Background**: *Helicobacter pylori* (*H. pylori*) infection has been shown to introduce DNA damage response (DDR) and autophagy in gastric epithelial cells. Autophagy, an intracellular degradation system, has been associated with DDR. In this study, we determine the exact mechanism and role of autophagy and DDR in the pathogenesis of *H. pylori* infection.

**Methods**: The effect of *H. pylori* infection on DDR and autophagy were examined in vitro co-culture system, in vivo murine models and human gastric biopsies. We observed the regulation of DDR pathway by autophagy in *H. pylori*-infected gastric cells. Furthermore, we evaluated determine the interaction between autophagy substrate P62 and DNA repair protein Rad51.

**Results**: Constant induction of DNA damage and reduction of autophagy have been found in gastric lesions. *H. pylori* infection significantly induced DNA damage and inhibited DNA repair protein Rad51 expression in gastric epithelial cells and Mongolian gerbils. Interestingly, we found that autophagy levels increased early and then decreased gradually after *H. pylori* infection. Mechanistically, loss of autophagy led to aggravate DDR in *H. pylori*-infected cells. Furthermore, knockdown of P62 remarkably increased Rad51 expression. P62 has been shown to promote Rad51 ubiquitination via its UBA domain.

**Conclusions**: Our findings indicated that in response to *H. pylori* infection loss of autophagy resulted in the accumulation of P62, which induced ubiquitination and degradation of DNA repair protein Rad51. Reduced Rad51 caused persistent DNA damage, which contributes to *H. pylori*-infected gastric carcinogenesis. This study provided a novel mechanism between *H. pylori* infection, autophagy, DNA damage and gastric tumorigenesis.

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## W2.4 | The innate immune molecule NLRC5 protects against Helicobacter-induced gastric B cell lymphomagenesis

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The inflammation generated by *Helicobacter pylori* infection is directed at clearing the bacterium, but can be harmful to the host. *H. pylori* has developed several strategies to attenuate excessive host inflammation. We have identified a new mechanism whereby *H. pylori* is able to dampen inflammation via its targeting of the NOD-like receptor (NLR) family member, NLRC5, in myeloid cells. In response to *Helicobacter* stimulation, *NLRC5* expression was upregulated in both mouse and human macrophages to levels comparable to those for known NLRC5 agonists i.e. LPS, IFN-g. *Nlrc5*/*NLRC5* expression was also significantly upregulated in response to infection in gastric tissues ($P < 0.01$) and correlated positively with disease severity in human biopsies ($P < 0.05$). In response to *Helicobacter* stimulation, *NLRC5* CRISPR knockout (KO) macrophages displayed significantly greater cytokine/chemokine responses than wild type (WT) cells. At 3 months post-infection, mice lacking *Nlrc5* in the myeloid cell compartment exhibited splenomegaly ($P < 0.0001$), gastric hyperplasia ($P < 0.0001$) and increased serum antibody titres ($P < 0.01$), when compared with WT animals. Importantly, conditional *Nlrc5* KO mice also exhibited increased numbers of gastric $CD19^+$ B cell

lymphoid follicles ($P < 0.0001$) resembling the precursor lesions of B cell mucosa-associated lymphoid tissue (MALT) lymphoma. We identified the B-cell activating factor, BAFF, to be a key promoter of the hyperproliferative activity of B cells in *Nlrc5* KO mice. In conclusion, we propose that macrophage-derived NLRC5 acts as a regulator of pro-inflammatory responses to *Helicobacter* infection and, moreover, that aberrant NLRC5 signalling may be a factor in the development of *H. pylori*-associated gastric MALT lymphoma.

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## W2.5 | DNA hypermethylation downregulates Telomerase Reverse Transcriptase (TERT) during *H. pylori*-induced chronic inflammation

F. I. Bussière[1]; V. Michel[2]; J. Fernandes[2]; L. Costa[2,3]; V. Camilo[2]; H. De Reuse[2]; L. Fiette[2,4]; **E. Touati**[2]

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*Helicobacter pylori* is responsible for 90% of gastric cancer cases. During *H. pylori*-induced inflammation, reactive oxygen species (ROS) promote genetic instability. *H. pylori* also induces DNA hypermethylation. Telomerase is essential to maintain telomere length and chromosome integrity. Its major component, the telomerase reverse transcriptase (TERT), is an important target for pathogens. We aimed to investigate the consequences of *H. pylori* on TERT level and telomerase activity. *In vitro*, *hTERT* mRNA levels and telomerase activity were analysed in *H. pylori*-infected human gastric cells. In addition, the influence of *H. pylori*-induced inflammation on TERT levels was investigated in mice. Our data demonstrated that *H. pylori* inhibits the *TERT* gene expression and decreases the telomerase activity in gastric cells. Exposure of infected cells to the antioxidant lycopene, abolished this downregulation, suggesting a ROS-mediated effect. *In vivo*, lower m*TERT* expression and TERT-positive cells are confirmed in gastric tissues of infected mice compared to non-infected, specifically in the vicinity of lymphocyte aggregates, suggesting an inflammation-mediated regulation. PCR-methylation analysis on CpG islands of the *mTERT* promoter, showed a DNA hypermethylation in infected mice. The involvement of DNA hypermethylation in the *H. pylori*-mediated downregulation of *TERT* gene expression was confirmed *in vitro*, by the restoration of *TERT* transcript levels in infected cells treated with 5′-azacytidine, a DNA methylation inhibitor. Our data unraveled a novel way for *H. pylori* to promote genome instabilities through the inhibition of TERT levels and telomerase activity. A mechanism that could play an important role in the early steps of gastric carcinogenesis.

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## W2.6 | *Helicobacter pylori* dampens MHC-II expression on macrophages via the up-regulation of miRNAs targeting CIITA

**M. de Bernard**; G. Codolo; M. Toffoletto; F. Chemello; S. Coletta; G. Soler Teixidor; G. Battaggia; G. Munari; M. Fassan; S. Cagnin

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Macrophages have a major influence on inflammation, pathology and disease and the available data suggest that *H. pylori* persistence can be explained in part by the failure of the bacterium to be killed by professional phagocytes. Macrophages are cells ready to kill the engulfed pathogen, through oxygen-dependent and -independent mechanisms; however, their killing potential can be further augmented by the intervention of T helper (Th) cells upon the specific recognition of MHC-II-peptide complexes on the surface of the phagocytic cells. As it pertains to *H. pylori*, the bacterium is engulfed by macrophages, but it interferes with the phagosome maturation process leading to phagosomes with an altered degradative capacity, and to megasomes, wherein *H. pylori* resists killing. We recently shown that macrophages infected with *H. pylori* strongly reduce the exposure of MHC-II molecules on the plasma membrane and this compromises the bacterial antigen presentation to Th lymphocytes. In this work, we demonstrate that *H. pylori* hampers MHC-II expression in macrophages, activated or non-activated by IFN-γ, by down-regulating the expression of the class II major histocompatibility complex transactivator (CIITA), the "master control factor" for the expression of MHC class II genes. We evidenced that this effect relies on the up-regulation of Let-7f, let-7i, miR-146b and -185 targeting CIITA. A meta-analysis approach and the quantification of miRNA expression in the gastric mucosa of *H. pylori*-infected patients, supported the notion that let-7i-5p, miR-185-5p and -146b-5p might be involved in the onset of gastritis and in the subsequent stages of pre-neoplastic and neoplastic conditions.

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## W2.7 | *H. pylori* epigenome micro-evolution associated with DNA methyltransferases' sequence-specificity changes

**M. Fukuyo**[1,2]; H. Yano[3,4]; H. Yonezawa[5]; N. Takahashi[5]; K. Yahara[6]; M. Konno[7]; T. F. Shibata[8]; S. Shigenobu[8]; B. Rahmutulla[1]; I. Uchiyama[8]; Y. Hasegawa[2]; O. Ohara[2]; A. Kaneda[1]; I. Kobayashi[3,5,9]

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Works with *H. pylori* have suggested the possibility that adaptive evolution may proceed through selection from a variety of methylomes (epigenomes), as opposed to a variety of genomes. Earlier, we knocked out a dozen of its DNA methyltransferases and analyzed methylome, transcriptome and adaptive phenotype sets (motility, ROS tolerance, DNA damage tolerance…), which demonstrated that many DNA methyltransferases served as hub transcription factors of a gene regulation network and, furthermore, suggested that these methyltransferases frequently changed their sequence specificity to remodel the network for adaptive evolution (FIREWORK model; H. Yano et al. in prep.). Here, we analyzed strains sampled from family members for methylome micro-evolution. In 1st family, methylation motifs overlapped completely. In 2nd family, a unique Type III methylation motif was found in only one child, and its target genes were highly enriched in the functional category of Metabolic Pathways (KEGG). They included an operon-like cluster for lipopolysaccharide synthesis. In 3rd family, changes in many methylation motifs including a set of related Type I methylation motifs were found. We were able to reconstruct evolution of the latter by a single amino-acid substitution, intra-molecular deletion and gene conversion in their specificity subunit genes. Among the genes uniquely methylated/unmethylated in the child were those for outer membrane proteins, multi-drug transporters, biosynthesis, and chemotaxis. The emerging picture of methylome micro-evolution supports our FIREWORK model for *H. pylori* and the concept of epigenome-driven adaptive evolution in general.

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# WORKSHOP W3 TREATMENT OF HELICOBACTER INFECTION I

## W3.1 | Is *Helicobacter pylori* cure a life-long strategy? A 25 years survey on 693 patients

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**Background and Aim**: Few studies deal with H.p. free status after eradication. This study aims to evaluate relapse rate in a group of 693 patients, after a successful cure, in a long follow-up period.

**Materials and Methods:** Overall, 693 (M: 421, mean age: 43 yrs, range: 18-65 yrs) consecutive H.p.+ patients were, from 1992 to 1994, divided into 3 groups by diagnosis: 315 with Duodenal Ulcer (DU), 196 Gastric Ulcer (GU) and 182 non-atrophic chronic gastritis (NACG). Everyone underwent EGD with biopsies, (Sidney System), at baseline, to provide the diagnosis and detecting H.p. (and CAG A+/CAG A- status), an UBT, determination of serum IgG anti-H.p., treated with 7-days Triple Therapy (Omeprazole, Amoxycilline and Clarytromicine or Omeprazole, Amoxycilline and Tinidazole) for eradication, confirmed by UBT, EGD and serology at 2 months, 6 months and 1 year. Patients were followed-up for 25 years, undergoing UBT every 5 years, at least 2 (2-9) EGD with biopsies, and serology every 2 years.

**Results**: Results are shown in table 1. 76 relapses were detected in 25 years (11%).No statistical ($P > 0.5$) difference was assessed between DU, GU and NACG group, sexes, type of treatment or CAG A+ and CAG A- status.

**Conclusions**: Relapse rate in long-term follow-up after H.p. cure is consistently low (2.5% every 5 years). This feature represents an evidence for H.p. eradication, life-long in most patients.

**TABLE 1**

| Years of follow-up | N° of relapses | % of relapses |
|---|---|---|
| 0-5 | 27 | 3.89 |
| 5-10 | 13 | 1.87 |
| 10-15 | 16 | 2.31 |
| 15-20 | 11 | 1.59 |
| 20-25 | 9 | 1.30 |

F. Di Mario: None. A. Barchi: None. M. Russo: None. M. Franceschi: None. N. Dal Bò: None. R. Cannizzaro: None. C. Miraglia: None. A. Tursi: None. G. Brandimarte: None. P. Crafa: None. L. Franzoni: None. M. Rugge: None.

## W3.2 | High efficacy of 14-day high-dose PPI bismuth-containing quadruple therapy with probiotics supplement for *Helicobacter pylori* eradication in high clarithromycin resistance areas: A double blinded-randomized placebo-controlled study

**P. Poonyam**[1,2]; R. Vilaichone[2,3,4]; P. Chotivitayatarakorn[2,3,4]; V. Mahachai[3]

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**Background**: Bismuth-containing quadruple therapy has recently been the first line regimen recommended in many European countries but limited efficacy in ASEAN especially Thailand. High-dose PPI bismuth-containing quadruple therapy plus probiotic has never been evaluated the efficacy in this high prevalence area of *H. pylori* infection and clarithromycin resistance.

**Methods**: In this double-blind randomized placebo-controlled study, *H. pylori* infected patients were randomized to receive 7- or 14-day high dose PPI bismuth-containing quadruple therapy(60 mg dexlansoprazole twice daily,1048 mg bismuth subsalicylate twice daily,500 mg tetracycline four times daily,400 mg metronidazole three times daily. with or without probiotics(37.5 mg Lactobacillus reuteri (BioGaia®) twice daily) supplement. *H. pylori* eradication was defined as negative 13C-UBT 4 weeks after treatment.

**Results**: 100 subjects were enrolled (72 females,28 males, mean age = 54 years). Antibiotic resistance was 15.6% for clarithromycin, 34.1% for metronidazole CYP2C19 genotyping revealed 37% rapid, 50%intermediate and 13% poor metabolizers. Overall eradication rates of 14-day was significantly higher than 7-day regimens (70% vs 92%; *P*-value = 0.005). The eradication rate for all patients with poor and rapid metabolizers were 100% with 14-day regimen. 14-day regimen with probiotics can also achieve 100% eradication rate for clarithromycin, metronidazole and dual resistances. Incidence of treatment side effects including N/V, abdominal discomfort and bitter taste were significantly lower in patients with probiotics than placebo (6% vs 26%: *P* = 0.002; OR = 0.13; 95% CI = 0.03-0.53, 4% vs 18%: *P* = 0.017; OR = 0.16; 95% CI = 0.03-0.81, and 4% vs 26%; *P* = 0.001: OR = 0.08; 95% CI = 0.016-0.41, respectively)

**Conclusions**: 14-day high dose PPI bismuth-containing quadruple therapy provide excellent *H. pylori* eradication rate regardless of CYP2C19 and antibiotic resistance. Adding probiotic also significantly reduced treatment adverse events and improve the patients' compliance.

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## W3.3 | The comparison of effectiveness of standard triple therapy and high-dose amoxicillin/ bismuth therapy in eradication of *H. pylori*

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[1]*Faculty of Medicine, University of Latvia, Riga, Latvia;* [2]*Institute of Clinical and Preventive Medicine, University of Latvia, Riga, Latvia;* [3]*Latvian Biomedical Research and Study centre, Riga, Latvia;* [4]*Digestive Diseases Centre GASTRO, Riga, Latvia*

**Background**: Antibiotics are the standard treatment for *Helicobacter pylori* infection. A standard triple therapy including Clarithromycin leads to persistent macrolide resistance in normal microbiota, and tends to cause wide spectrum of side effects. Objective: to compare effectiveness of standard triple therapy (Amoxicillin 1 g x2, Clarithromycin 0.5 g x2 and Esomeprazol 0.04 g x2 - 10 or 14 days) and non-macrolide high-dose amoxicillin/bismuth therapy (Amoxicillin 1 g x3, Esomeprazol 0.04 g x2 and Bismuth subcitrate 0.24 g x2 - 14 days), and to evaluate patients' compliance to regimens.

**Methods**: Clinical trial participants were healthy individuals aged 40-64. Eradication subgroup underwent urea breath test (UBT); positive patients were randomly divided into eradication subgroups. Control group included patients with unknown *H. pylori* status. Patients were contacted in 21-28 days after therapy; side effects and patients' compliance were registered. Control UBT was performed after six months. Participants also provided stool samples before and six months after for microbiome analysis.

**Results**: Overall, 2341 patients participated. By now, follow-up UBT underwent 777 patients (33.2%). Standard 10-day therapy was effective in 87.8% (115/139), standard 14-day - in 87.8% (86/98) and alternative therapy - 78.2% (79/101). There was no significant difference of effectiveness between therapy regimens (*P* = 0.169, $Chi^2$=6.4). Moreover, the compliance to alternative therapy due to fewer side effects was higher: 96.3% vs 93.2% in 14-day-triple and 94.2% in 10-day-triple ($Chi^2$=4.1). Compliance was associated with therapy effectiveness (*P* = 0.002).

**Conclusions**: Reduction of antibiotic use may avoid resistance growth, have positive effect on patients` compliance and foreseeable lower impact on microbiota by alike effectiveness.

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## W3.4 | A multi-center real-life study on comparison between bismuth quadruple (BQ) (10 days) and clarithromycin (CLA) containing non-bismuth quadruple (CT) therapy (10 and 14 days) in the eradication of *H. pylori* infection in patients naïve to treatment in a region with high CLA and dual resistance

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**Aim**: We evaluated the efficacy of BQ vs CLA-containing CT (10d or 14d) in *H. pylori*-infected subjects naïve to treatment in an area of high CLA and dual (CLA+metronidazole) resistance. Patients who had previously been exposed to CLA were given BQ whereas those who had not were given CT. In Italy BQ is only possible through the 3-in-1pill (TiOP) formulation for 10d.

**Methods**: 201 patients received BQ (esomeprazole 40 mg bid+TiOP 3 tablets qid), 100 patients received CT (esomeprazole 40 mg bid+CLA 500 mg bid+amoxicillin 1 g bid+tinidazole 500 mg bid) for 10d and 103 patients CT for 14d. *H. pylori* infection was diagnosed through $^{13}$UBT or histology. Treatment-related adverse events (TRAEs) were evaluated by a questionnaire. Significance of differences was assessed by Chi square test.

**Results**: 1) ITT and PP eradication rates in BQ were 184/201 (91.5%, 95%CI 86.8-95) and 183/191 (95.8%; 85% CI 91.9-98.2), respectively; 2) ITT and PP eradication rates in CT10d were 80/100 (80%; 95% CI 70.8-87.3) and 80/94 (85.1%; 95% CI 76.3-91.6), respectively; 3) ITT and PP eradication rates in CT14d were 99/103 (96.1%; 95% CI 90.3-98.9) and 97/100 (97%; 95% CI 91.5-99. 4), respectively; 4)BQ and CT14d were significantly ($P < 0.001$) superior to CT10d. 5) TRAEs and TRAE-related treatment discontinuation were similar between regimens (p:ns).

**Conclusions**: 1) In an area of high prevalence of CLA and dual resistance BQ and CT14d are equally effective and safe in eradicating *H. pylori* infection and significantly superior to CT10d; 3) Prescribing therapy based on knowledge of previous exposure to CLA may represent a winning strategy.

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## W3.5 | Antibiotic-free lipid nanoparticles for gastric infection management

C. L. Seabra[1,2,3]; P. Parreira[1,2]; P. Henriques[1,2]; C. Monteiro[1,2]; J. Gomes[1,4]; I. Amorim[1,4,5]; F. Gartner[1,4,5]; C. Machado[1,2]; C. Nunes[6]; S. Reis[6]; E. Touati[7]; C. A. Reis[1,4,8]; I. C. Gonçalves[1,2]; **M. L. Martins**[1,2,5]

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*Helicobacter pylori* (*Hp*) infects the gastric mucosa of a large percentage of the human population worldwide and predisposes to peptic ulceration and gastric cancer[1]. Current treatment shows a rapid decline of *Hp* eradication rates, mainly due to high bacterial resistance rates to available antibiotics[2].

We propose a new therapeutic approach based on docosahexaenoic acid (DHA). This polyunsaturated fatty acid has high bactericidal activity against *Hp*[3] but low *in vivo* efficacy. To overcome this drawback, we developed lipid nanoparticles loaded with DHA (DHA-LNPs). DHA-LNPs had improved bactericidal performance against *Hp* (vs free DHA) and didn't affect gut microbiota (*in vitro* testing)[4,5].

*In vivo* efficacy (mice model) was accessed with two administration modes: oral gavage and *ad libitum*. DHA-LNPs concentration for both administration modes was 50 μM/day. Independently of the administration mode, DHA-LNPs reduced 90% of bacterial colonization. It is noteworthy in *ad libitum* administration, the total amount is divided by six mice/cage, meaning that each animal only ingested 2- 3 μM of DHA-LNP/day. This observation highlighted that multiple doses of therapy could be more beneficial. Toxicity assays revealed that DHA-LNPs are biocompatible and well-tolerated by mice.

In conclusion, DHA-LNPs emerge as a highly promising antibiotic-free therapy for *Hp* gastric infection management.

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## W3.6 | Fate of meta-analyses: the case of *Helicobacter pylori*

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**Background**: Meta-analyses of randomised controlled trials constitute the highest level of medical evidence.

**Aim**: To analyse the implementation of meta-analyses in the major guidelines of the management of *Helicobacter pylori* infection.

**Methods**: The full texts of major international and national consensus guidelines published were retrieved from the MEDLINE and the cited meta-analyses from the reference lists were identified and their percentage in the total number of references was calculated.

**Results**: Citation rate of meta-analyses in the national and international consensus guidelines for the management of *Helicobacter pylori* infection.

**Conclusions**: The implementation of meta-analyses in current guidelines is rather weak and probably insufficient. A more extensive use of meta-analyses is recommended in formulating statements and recommendations, otherwise their continuous publication will lose purpose and scientific significance, being performed in vane.

G.M. Buzás: None.

| Year | Consensus conference | No. of references | No. and % of meta-analyses |
|---|---|---|---|
| 1996 | Maastricht I | 55 | 0 (0%) |
| 2002 | Maastricht II | 100 | 2 (2%) |
| 2007 | Maastricht III | 99 | 10 (9.9%) |
| 2007 | AGA | 175 | 23 (13.1%) |
| 2009 | II.Asian-Pacific | 118 | 12 (10.2%) |
| 2012 | Maastricht IV-Florence | 325 | 36 (11.1%) |
| 2016 | Maastricht V - Florence | 416 | 53 (12.7%) |
| 2017 | Toronto | 140 | 24 (17.1%) |
| 2017 | Ireland | 100 | 12 (12%) |
| 2017 | AGA | 217 | 28 (12.8%) |
| 2017 | S2K Guideline, Germany | 472 | 53 (11.1%) |
| 2018 | IV. Braziliaan | 216 | 25 (11.6%) |
| 2018 | V. Chinese | 175 | 20 (11.4%) |
| 2018 | IV. Mexican | 122 | 13 (10.6%) |
| | **Total** | **2730** | **311 (11.39%)** |

## W3.7 | Pan-European Registry on *H. pylori* management (Hp-EuReg): Analysis of 4,388 second-line treatments

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**Introduction**: After a failed eradication attempt, *H. pylori* treatment's efficacy is compromised.

**Aims**: To evaluate the efficacy of second-line *H. pylori* treatments.

**Methods**: A systematic prospective registry of the clinical practice of European gastroenterologists regarding *H. pylori* infection and treatment. *Variables included:* patient's demographics, previous eradication attempts, prescribed eradication treatment, adverse events, and outcomes (cure rates, compliance, follow up). *Analysis:* Cases with an empiric treatment after just one eradication attempt were evaluated separately from those with a tailored therapy.

**Results**: Overall, 4,388 second-line patients were included. In total, 4,019 were treated empirically: Mean efficacy was 77% (by ITT) and 83.5% (by PP). 7 and 10-days regimens did not reach optimal efficacy except for single-capsule bismuth quadruple therapy (>90% PP). 14-days regimens with double doses esomeprazole reported better results (>90% PP) when quinolones were used in triple regimens and bismuth quadruple therapies. After non-bismuth quadruple failure, efficacy was higher when the triple therapy with moxifloxacin or the bismuth quadruple therapy with levofloxacin were used. Over 97% of patients were compliant. Adverse events were reported in 29% of the cases and tolerance was similar among therapies.

**Conclusion**: Second-line triple therapies generally provide low eradication rates except when prescribing moxifloxacin for 14 days. Bismuth-containing quadruple therapies seem to provide higher efficacy, especially the combination of bismuth with a PPI, levofloxacin and amoxicillin or the single-capsule bismuth quadruple therapy.

| Most frequent 2nd line treatments | N | % Use | N (ITT) | ITT (%) | (95% CI) | N (PP) | PP (%) | (95% CI) |
|---|---|---|---|---|---|---|---|---|
| Triple-A+L | 1,449 | 36.1 | 1,349 | 77 | (75-79) | 1,271 | 81 | (79-83) |
| Pylera | 510 | 12.7 | 466 | 87 | (84-90) | 442 | 91 | (88-94) |
| Quadruple-A+L+B | 459 | 11.4 | 446 | 88 | (85-91) | 421 | 90 | (87-93) |
| Triple-C+A | 414 | 10.3 | 358 | 51 | (46-56) | 221 | 79 | (74-84) |
| Quadruple-M+Tc+B | 179 | 4.5 | 167 | 81 | (75-87) | 158 | 84 | (78-90) |
| Quadruple-C+A+M | 145 | 3.6 | 133 | 83.5 | (77-90) | 131 | 84 | (78-90) |
| Triple-A+Mx | 140 | 3.5 | 138 | 88 | (83-93) | 134 | 91 | (86-96) |
| Triple-A+M | 85 | 2.1 | 79 | 56 | (45-67) | 73 | 59 | (48-70) |
| Total | 3,966 | 98.7 | 3,689 | 77 | (76-78) | 3,346 | 83 | (82-84) |

ITT, intention to treat; PP, per-protocol; 95%CI, 95% confidence interval; PPI, proton pump inhibitor; C, clarithromycin; M, metronidazole; T, tinidazole; A, amoxicillin; L, levofloxacin; B, bismuth salts; Tc, tetracycline; Mx, moxifloxacin; N, Total of patients receiving an empiric treatment.

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## W3.8 | Current treatment of *Helicobacter pylori* infected children and adolescents in Europe: Interim Results of the new EuroPed*Hp* Registry

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**Aims**: The new EuroPed*Hp* registry was initiated by the *H. pylori* working group of ESPGHAN to surveil antibiotic resistance, to assess current practice of *H. pylori* therapy and to evaluate eradication success according to the updated ESPGHAN and NASPGHAN Guidelines *(JPGN 2017;64: 991-1003).*

**Methods**: Since 2017, 30 centers from 17 European countries prospectively reported demographic, clinical and follow up data of pediatric patients diagnosed with *H. pylori* infection by invasive or non-invasive tests.

**Results**: Of 1069 submitted cases, 618 (51.3% female, median age 13.0, 5.7% with peptic ulcer) provided treatment and follow up data to determine eradication rate (ER); 524 were treatment naïve (group A), 94 had failed previous therapy (group B). Strains susceptible to clarithromycin (CLA) and metronidazole (MET) were detected in 57.2% (A: 60.7%, B: 36.6%), double-resistance to both drugs in 7.1% (A: 5.2%, B: 18.3%). Primary resistance to CLA and/or MET was high (26.8%, 17.8%, respectively, $P < 0.001$). Almost 80% received tailored triple therapy (TT) with PPI+Amoxicillin (AMO)+CLA (41.2%) or PPI+AMO+MET (38.3%), thereof 95.3% for 14 days. Antibiotics were dosed according to guidelines in >80%, while PPI dose was lower than recommended in 57%. In fully susceptible group A patients, ER tended to be higher with tailored TT with PPI+AMO+CLA or PPI+AMO+MET than with sequential therapy (91%, 94.6% vs 85.7%, respectively). ER in group B patients reached 63.1%.

**Conclusion**: In treatment naïve patients, TT for 2 weeks tailored to antibiotic susceptibility testing achieved an ER close to the 90% goal. Increasing PPI dose may further improve treatment success.

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# WORKSHOP W4 GASTRIC CARCINOGENESIS

## W4.1 | UNDERSTANDING THE TUMOUR-PROMOTING FUNCTIONS OF AUTOPHAGY IN GASTRIC CARCINOGENESIS

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**Background**: We have previously demonstrated that highly virulent *Helicobacter pylori* strains modulate autophagy in both immune and nonimmune cells. We now aimed at elucidating the role of autophagy in *H. pylori*-related gastric cancer (GC) by assessing the association between autophagy-related genetic polymorphisms and gastric carcinogenesis in a unique cohort comprising 1039 individuals from diverse ethnic groups, geographical locations and with varying GC risks, and by deciphering their biological significance using genome editing in gastric epithelial cells.

**Methods**: The study sample included 1039 subjects (Australians: 119 GC and 236 controls; Colombians: 89 and 293 controls; ethnic Chinese: 86 and 216 controls). DNA was extracted from peripheral whole blood and customised SNP genotyping was performed using the Agena Bioscience MassARRAY assay. Statistical analyses included bivariate, multivariate, joint-analyses and meta-analyses. A CRISPR/Cas9 system was employed to introduce *IRGM*-rs4958847 in gastric epithelial cells. Editing was validated using genome cleavage detection, qPCR and Sanger sequencing, and infection with *H. pylori* was assessed in this model.

**Results**: In multivariate analyses, autophagy-related polymorphisms (*ATG2B*-rs3759601, *ATG5*-rs2245214, *ATG16L1*-rs2241880,

*IRGM*-rs4958847, *mTOR*-rs1883965, *ULK*-rs12303764) significantly modulated GC risk in Australians, Colombians and ethnic Chinese. Of these, *IRGM* and *ATG16L1* polymorphisms markedly increased the risk of GC in ethnic Chinese- and Australians infected with *H. pylori*. *IRGM*-rs4958847-edited cells showed modulation of autophagy and impaired immune responses against *H. pylori* compared to wild-type cells.

**Conclusion**: Germ-line mutations within the autophagy pathway that were found to increase the risk of developing GC in three diverse human populations, modulate the epithelial response to *H. pylori* infection.

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## W4.2 | Molecular characterization of the gastric commensal bacteria progressing gastric carcinogenesis in *H. pylori*-infected gastric mucosa

**H. TsugaWa**[1]; J. Matsuzaki[1]; H. Mori[2]; M. Suematsu[1]; H. Suzuki[3]

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**Objective**: Recent studies show that development of gastric cancer also requires commensal bacterium other than *H. pylori*. However, it is uncertain how commensal bacterium is involved in gastric carcinogenesis because the non-*H. pylori* pathobiont has not been identified. The present study was conducted to examine the role of gastric microbiota in the development of gastric cancer and to identify the non-*H. pylori* pathobiont.

**Methods:** *H. pylori*TN2GF4 strains were inoculated to mice for the development of *H. pylori* infection model. A sequencing library of the 16S rRNA gene V3-V4 regions was established by using extracted DNA from gastric contents, and then sequencing reaction was performed with a MiSeq Illumina instrument. Short chain-fatty acids (SCFAs) in gastric lumen were measured by LC-MS.**Results**: Recently, we showed that CagA oncoprotein specifically accumulated in CAPZA1-overexpressing cells (*AutoPhagy* 15:252, 2019). Cancer stem cell marker CD44v9 expression was evoked in CAPZA1-overexpressing cells following CagA accumulation. Indeed, CD44v9 expressions were colocalized with CAPZA1-overexpressing cells in human gastric cancer tissues. SCFAs induced CAPZA1 expression by increasing acetylation of *CAPZA1* promoter regions. These findings show that SCFAs promote the development of CAPZA1-overexpressing cells, leading to the development of CD44v9-positive gastric cancer stem-like cells. As a result of searching for SCFA-producing gastric commensal bacteria in *H. pylori*-infected gastric mucosa, we identified *Lachnospiraceae* sp., which is known to be significantly increased in patients with gastric cancer.

**Conclusion**: Our findings demonstrate that SCFAs overproduced by *Lachnospiraceae* sp. would induce gastric cancer by increasing CAPZA1-overexpressing cells in *H. pylori*-infected gastric mucosa.

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## W4.3 | *Helicobacter pylori*-activated gastric fibroblasts induce permanent reprogramming of gastric epithelial cells towards invasive phenotype in vitro

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**Background**: Metastasis is the most fatal consequence of gastric cancer (GC). The epithelial to mesenchymal transition (EMT) allows the tumor cells to acquire invasive properties and to develop metastatic growth characteristics. Aim: to determine the long-term consequences of Hp (cagA+vacA+) infection-activated gastric fibroblasts and normal gastric epithelial cells on their EMT-related metastatic potential in vitro.

**Methods**: RGM-1 cells were cultured in the supernatants from Hp-infected fibroblasts for 30 days, assessed by Transwell invasion assay degradation 3D of extracellular matrix, MMP2, MMP9, MMP3 and FAP mRNAs in RGM-1 cells.

**Results**: Hp infection triggered GF activation into cancer-associated fibroblast (CAF)-like phenotype characterized by strong up-regulation of NF kappaB and STAT3 mRNA. The prolonged RGM-1 exposition to Hp-induced CAFs supernatant increased MMP9 and MMP2 mRNA levels and elicited MMP3 and FAP mRNA expression in normal epithelial cells, which correlated with their ability to migrate through and to degrade 3D ECM. Pro-invasive potential of RGM-1 cells was accompanied by induction of HGF production in these cells.

**Conclusion**: Normal gastric fibroblasts infected with Hp in STAT3 and NFkappaB-dependent manner, are sufficient not only to induce short-term EMT-related gastric epithelial cell responses but also to trigger their permanent reprogramming towards invasive and potentially important metastatic phenotype.

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## W4.4 | Identification of novel serological biomarkers for gastric cancer in the MCC-Spain case-control study based on *Helicobacter pylori* whole-proteome microarrays

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The humoral immune system of a *Helicobacter pylori (H. pylori)* infected individual responds to different antigens of the pathogen by eliciting a variety of antibodies. Based on differential bacterial protein expression, these antibody responses may represent infection- or disease-specific patterns. Previously published approaches to measure *H. pylori* antibody patterns have only utilized a small fraction of its 1445 encoded proteins.

We recently developed a method to produce bacterial whole-proteome microarrays and were able to successfully adapt this method to generate *H. pylori* whole-proteome microarrays representing 90% of the entire *H. pylori* (strain 26695) proteome. In an initial screen, serum samples from gastric cancer cases and *H. pylori*-infected, but cancer-free controls (each n = 60) from the MCC-Spain case-control study were pooled and analyzed for differential antibody patterns.

We identified published antigens such as GroEL and NapA as general *H. pylori* infection markers with all tested serum pools. However, newly identified antigens, such as the co-chaperone GroES (HP0011) and 3-dehydroquinate dehydratase (HP1038) showed even stronger reactivities.

Serum antibodies to the outer membrane proteins HP1564, HP0923 and HP0229, neuraminyllactose-binding hemagglutinin (HP0797) and the flagellar biosynthesis regulator FlhF (HP1035) were strongly associated with gastric cancer in first microarray analyses. Results were confirmed by analyzing single sera on minimized microarrays.

Validation of published antigens and the identification of new gastric-cancer associated antigens indicates that whole-proteome microarrays are a useful tool for unbiased antigen identification in the search for gastric cancer associated biomarkers.

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## W4.5 | Risk of progression of intestinal metaplasia in a low gastric cancer incidence country

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**Introduction**: Gastric cancer (GC) is the second leading cause of cancer-related death in the world. Most gastric adenocarcinomas are preceded by a cascade of well-defined precursor lesions, including intestinal metaplasia (GIM) and dysplasia. We aimed to investigate the rates of progression of GIM to dysplasia and GC in a low incidence country.

**Methods**: All patients with GIM detected at gastroscopy in Tallaght University Hospital from 2008 to 2012 were identified in the hospital database. Follow-up data were evaluated until 31st December 2018. I

**Results**: In total, 933 patients with GIM were identified between 2008 and 2012 and 42.2% (394) of them had follow-up in the defined period. 207 males (53%) and 187 females (47%) were followed up. Mean age at which GIM was diagnosed was 62 years. Over the follow-up period 12 patients had progression to either GC (8) or dysplasia (4). This equates to progression in 1.3% of all GIM diagnoses and 3% of those followed up over 5 to 10 years.

**Conclusions**: Our results suggest that in this low GC incidence cohort, risk of progression from GIM to GC is comparable to low risk Barrett's lesions, reinforcing the need to consider appropriate surveillance protocols.

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## W4.6 | Prevention of *Helicobacter pylori*-associated gastric carcinogenesis with dietary walnut

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n-3 polyunsaturated fatty acid such as EPA and DHA is known to be beneficial nutraceuticals plentiful in fish, nut, and krill. Since we have published fat-1 transgenic mice over-expressing 3-desaturase significantly mitigated *H. pylori*-associated gastric pathologies including rejuvenation of chronic atrophic gastritis and prevention of gastric cancer, in this study, under the hypothesis that dietary intake of walnut plentiful of n-3 PUFAs can be nutritional intervention to prevent *H. pylori*-associated gastric cancer. In our model that *H. pylori*-initiated, high salt diet promoted gastric carcinogenesis, 100 mg/kg and 200 mg/kg walnut contained pellet diet was administered up to 24 week and 36 weeks. As results, control mice

at 24 weeks developed significant pathologies including chronic atrophic gastritis and gastric adenoma in some. Dietary walnuts significantly ameliorated CAG in gross and histologic assessment, for which COX-2/$PGE_2$/NF-κB/C-*Jun*/STAT3, all elevated in control group, were all significantly decreased with walnut. Furthermore, tumor suppressive enzyme, 15-PGDH, was significantly preserved with walnut. Control mice at 36 weeks developed significant tumors accompanied with severe CAG. However, significantly decreased tumorigenesis was noted in group treated with walnuts, in which COX-2/PGE2/NF-κB/IL-6/C-Jun/STAT3, all elevated in control group, were all significantly decreased with walnut. On the other hand, the levels of HO-1, 15-PGDH, Nrf2, SOCS-1 were significantly increased in walnut treated group ($P < 0.01$). Proliferative index as marked with Ki-67 and PCNA was significantly regulated with walnut relevant to 15-PGDH preservation. Conclusively, dietary intake of walnut can be an anticipating nutritional intervention

K.B. Hahm: None. Y. Shin: None.

## W4.7 | Role of Leukaemia Inhibitory Factor (LIF) on the tumorigenic properties of Cancer Stem Cells in gastric adenocarcinoma

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**Introduction**: Cancer stem cells (CSCs), a small cell subpopulation having intrinsic chemo-resistance mechanisms and expressing CD44 cell surface glycoprotein, have been characterised in gastric adenocarcinoma (GC) and their link with the cell growth regulator pathway, Hippo/YAP/TEAD, has recently been suggested. Recent studies have defined Leukaemia Inhibitory Factor Receptor (LIFR) and LIF as being upstream regulators of the Hippo pathway and as being anti-metastatic in breast cancer. Interestingly, the impact of LIF on gastric CSCs has never been investigated.

**Aims & Methods**: Consequently, this study aimed to determine the effect of LIF supplementation on the YAP/TEAD pathway and CSC phenotype and properties in GC. The expression of Hippo/YAP/TEAD-related genes and CSC markers was assessed by RTqPCR, western blot and immunofluorescence analysis in GC cell lines (AGS and MKN45) and in patients-derived GC cells after LIF supplementation. YAP/TEAD transcriptional activity was evaluated by TEAD-luciferase reporter assay and proliferation as well as tumorsphere assays were carried out *in vitro* to evaluate CSC functional properties.

**Results**: LIF represses YAP/TEAD pathway through decreased YAP translocation to the nucleus and decreased expression of YAP/TEAD target genes. In addition, LIF decreases proliferation, tumorsphere initiation capacity and expression of gastric CSC markers.

**Conclusion**: Our results indicate that LIF presents anti-tumorigenic effects in GC. Whether the effect of LIF on CSC properties passes through the Hippo/YAP/TEAD pathway activation needs to be further investigated. This could *in fine* lead to the development of targeted strategies against CSCs, helping decrease the number of relapse cases and bad prognosis in gastric cancer.

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## W4.8 | IL-27 is abrogated in the gastric mucosa and serum of patients with gastric cancer in opposite to duodenal ulcer

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*Helicobacter pylori* (HP) infection is associated with two mutually exclusive diseases, gastric carcinoma (CG) and duodenal ulcer (DU), but the involved mechanisms remain unknown. IL-27 and plays a dual role in the immune response either stimulating Th1 or inhibiting Th17 cells that have a particular link with carcinogenesis. IL-27 has been also considered a potential treatment for cancer and we are unaware of studies evaluating IL-27 in gastric cancer. Therefore, we prospectively studied 110 HP-positive patients and 40 healthy blood donors (BD) as controls. We assessed serum and gastric concentrations of IL-27 and Th1/Th17 cell-associated cytokines by ELISA. IL-27Rα (receptor) mRNA expression in PBMC was evaluated by rtPCR. This is the first study to demonstrate that IL-27 is abrogated in GC patients in contrast to all the other HP-positive patients with DU/gastritis and HP-positive BD. The highest mean concentrations of IL-27 were observed in DU patients. Indicating that the IL-27 dual roles were expressed in the HP infection, the cytokine concentration positively correlated with the Th1 and negatively with Th17-associated cytokines. DU was significantly associated with increased gastric concentrations of IL-12p70 and IFN-γ, Th1 cytokines. Conversely, gastric levels of Th17 cell-associated cytokines (IL-1β, IL-6, IL-17A, IL-23 and TGF-β) were significantly higher in GC than in DU patients. IL-27Rα was highly expressed in PBMC stimulated with HP strains. IL-27 concentrations were not associated with virulent *cag*A/*vac*A status. In conclusion, although *H. pylori* infection is able to elicit IL-27 production, DU and GC have diametrically opposed cytokine patterns.

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## WORKSHOP W5 TREATMENT OF HELICOBACTER INFECTION II

### W5.1 | *Helicobacter pylori* acid acclimation: The evil duo of a pH-gated urea channel and a cytoplasmic urease

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*Helicobacter pylori*'s proton-gated plasma membrane urea channel and cytoplasmic urease are essential for its survival in the stomach. The channel is closed at neutral pH and opens at acidic pH to allow the rapid access of urea to cytoplasmic urease. Urease hydrolyzes urea into $NH_3$ and $CO_2$, neutralizing entering protons and thus buffering the cytoplasm even in gastric juice at a pH below 2.0. We determined the crystal structure of the channel, revealing six protomers assembled in a hexameric ring surrounding a central bilayer plug of ordered lipids. Both the channel and the protomer interface contain residues conserved in the AmiS/UreI superfamily, suggesting the preservation of channel architecture and oligomeric state in this superfamily. Predominantly aromatic or aliphatic side chains line the entire channel. Follow-up microsecond-scale unrestrained molecular dynamics studies provide a detailed mechanism of urea and water transport by the channel. More recently, we have determined the structure of the 1.1 MDa urease with a bound inhibitor to 2.3 Å using cryo electron microscopy.

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Cunha, E.S., Chen, X., Mills, D., Luecke, H. "Cryo EM Structure of *Helicobacter pylori* Urease with Bound Inhibitor at 2.3 Å Resolution".

H.L. Luecke: None. E. Cunha: None.

### W5.2 | Dual therapy with vonoprazan and amoxicillin is as effective as triple therapy with vonoprazan, amoxicillin and clarithromycin for eradication of *Helicobacter pylori*

**T. Furuta**; M. Yamade; T. Kagami; T. Suzuki; T. Higuchi; T. Uotani; S. Tani; M. Iwaizumi; Y. Hamaya; S. Osawa; K. Sugimoto

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**Backgrounds/Aims**: Vonoprazan is the first clinically available potassium competitive acid blocker (P-CAB). This class of agents provides faster and more potent acid inhibition than PPIs. Most strains of *Helicobacter pylori* (*H. pylori*) are sensitive to amoxicillin. We hypothesized that dual therapy with vonoprazan and amoxicillin would provide the sufficient eradication rate for *H. pylori* infection. To evaluate this, we compared the eradication rate by the dual vonoprazan/amoxicillin therapy with that by the standard triple vonoprazan/amoxicillin/clarithromycin therapy.

**Methods**: We compared the eradication rate by the dual therapy with vonoprazan 20 mg bid and amoxicillin 500 mg tid for 1 week (n = 56) with that by the triple therapy with vonoprazan 20 mg bid, amoxicillin 750 mg bid and clarithromycin 200 mg for 1 week (n = 56). Successful eradication was diagnosed using the $^{13}$C-urea breath test at 1-2 months after the end of eradication therapy.

**Results**: The intention-to-treat analysis of the eradication rate with dual vonoprazan/amoxicillin therapy was 92.9% (52/56), while that with the triple therapy was 91.1% (51/56). There were no statistically significant differences in incidences of adverse events related to the study regimens.

**Conclusion**: Vonoprazan-based dual therapy (vonoprazan 20 mg bid and amoxicillin 500 mg tid for 1 week provides an acceptable eradication rate of *H. pylori* infection without the need for second antimicrobial agents, such as clarithromycin.

T. Furuta: None. M. Yamade: None. T. Kagami: None. T. Suzuki: None. T. Higuchi: None. T. Uotani: None. S. Tani: None. M. Iwaizumi: None. Y. Hamaya: None. S. Osawa: None. K. Sugimoto: None.

### W5.3 | Ten-day concomitant, 10-day sequential, and 7-day triple therapy in first-line treatment of *Helicobacter pylori* infection: a randomized nationwide trial in Korea

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**Objective**: This large scaled nationwide study aimed to compare the efficacy and safety of the 10-day concomitant therapy (CT) and 10-day sequential therapy (SQ) with those of the 7-day clarithromycin-containing standard triple therapy (STT) as first-line treatment against *Helicobacter pylori* infection in the Korean population.

**Design**: This study was a multicenter, prospective, randomized, controlled trial. Patients with *H. pylori* infection were assigned randomly: 7d-STT (lansoprazole 30 mg, amoxicillin 1 g, and clarithromycin 500 mg twice daily); 10d-SQ (lansoprazole 30 mg and amoxicillin 1 g twice daily for the first 5 days, followed by lansoprazole 30 mg, clarithromycin 500 mg, and metronidazole 500 mg twice daily for the remaining 5 days); or 10d-CT (lansoprazole 30 mg, amoxicillin 1 g, clarithromycin 500 mg, and metronidazole 500 mg twice

daily). *H. pylori* eradication was confirmed by urea breath test after 4-6 weeks after the end of each treatment.

**Results**: In total, 1137 patients from 15 hospitals were included. The primary goal was eradication rates by ITT and PP analysis. The 10d-CT achieved a markedly higher eradication rate than the 7d-STT, whether using the ITT (81.2% vs 63.9%) or PP analysis (90.6% vs 71.4%). The eradication rate of the 10d-SQ was superior to that of 7d-STT (76.3% vs 63.9%, ITT analysis; 85.0% vs 71.4%, PP analysis) as well. There was little difference among the three treatment arms in adherence and serious side effects.

**Conclusion**: 10d-CT and 10d-SQ were superior to 7d-STT for standard first-line treatment and can be an alternative to 7d-STT in Korea.

B.J. Kim: None. H. Lee: None. J. Kim: None. J. Kim: None.

## W5.4 | Effect of previous nitroimidazole treatment on *Helicobacter pylori* eradication success

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**Background**: Prior nitroimidazole exposure may increase the likelihood of nitroimidazole-resistant *Helicobacter pylori (H. pylori)*. Current *H. pylori* treatment guidelines recommend that in the absence of susceptibility testing, patients with prior nitroimidazole exposure should not be treated with a nitroimidazole antibiotic. Data to support this recommendation are lacking. We aimed to examine the impact of prior treatment with a nitroimidazole antibiotic on the success of *H. pylori* treatment.

**Methods**: We searched the Clalit Health Services database to identify subjects 25-60 years-old who underwent a first-ever $^{13}$C-urea breath test (UBT) between 2010-2015. Patients who underwent a previous *H. pylori* stool antigen test or gastroscopy were excluded. Pharmacy dispensation data were retrieved.

**Results**: 1386 subjects (34.8% males, age 40.7 ± 10.7 years) received a nitroimidazole-containing regimen including 282 (20.4%) with prior nitroimidazole exposure. Successful eradication was achieved in 58.9% and 73.8% of subjects with and without prior nitroimidazole exposure, respectively (OR, 0.51; 95% CI, 0.39-0.67; $P < 0.0001$). Nitroimidazole exposure adversely impacted the success triple therapy with nitroimidazole, PPI *and* amoxicillin *or* clarithromycin (39.4% *vs* 63.4% and 54.4% *vs* 73.6%, $P < 0.01$, respectively), but not quadruple therapies. Following multivariate analysis, nitroimidazole exposure was significantly associated with eradication failure (OR, 1.89; 95% CI, 1.43-2.50; $P < 0.0001$). A greater time elapsed from nitroimidazole exposure and a lower cumulative nitroimidazole dose were observed in subjects with successful eradication ($P < 0.0001$ for both).

**Conclusion**: Nitroimidazole exposure may adversely impact the success of nitroimidazole-based triple therapy, but not quadruple therapy. Clinicians should conduct a thorough patient drug-history before administering empiric treatment for *H. pylori* infection.

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## W5.5 | Growing *H. pylori* resistance to standard antibiotic therapies identified from a phase 3 clinical trial of treatment naive patients in the United States

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**Background**: Current antimicrobial susceptibility data for *Helicobacter pylori* isolates from treatment of naive patient populations in the USA is lacking. A 2015 study from the Houston VAMC reported 16.4% clarithromycin and 20.3% metronidazole resistance. We report new susceptibility data from *Hp* isolates recovered from treatment naive patients in the Unites States.

**Methods**: Isolates from de-identified patients enrolled in a multicenter clinical trial were tested (2017-2018) for minimal inhibitory concentrations (MICs) by agar dilution using Clinical and Laboratory Standards Institute (CLSI) methods. CLSI and EUCAST (The European Committee on Antimicrobial Susceptibility Testing)) interpretive breakpoints were applied. MICs were obtained for amoxicillin, clarithromycin, metronidazole and rifabutin. The reference strain was ATCC43504.

**Results**: MICs were obtained for 356 isolates recovered at 55 centers (20 states) across the USA. Utilizing CLSI breakpoints, 62/356 (17.4%; 95% CI = 13.8-21.7%) isolates were clarithromycin resistant (MIC ≥ 1 μg/mL). Amoxicillin MICs were >0.125 μg/mL in 24/356 (6.7%; 95% CI 4.6-9.8%), and 155/355 (43.7%; 95% CI = 38.6-48.9%) had metronidazole MIC > 8 μg/mL. No isolate had rifabutin MIC ≥ 1 μg/mL. Thirty-seven (10.4%; 95% CI = 7.7-14.0%) had dual clarithromycin-metronidazole resistance. The $MIC_{90}$ was 0.125 μg/mL for amoxicillin, 8 μg/mL for clarithromycin, 64 μg/mL for metronidazole, and ≤0.008 μg/mL for rifabutin.

**Conclusion**: In our national study, we found similar clarithromycin (17.4%) but higher metronidazole resistance (43.7%) than reported in 2015. We also report an unprecedented rate of amoxicillin resistance (>6%). No rifabutin resistance was noted. These emerging resistance patterns support the development of rifabutin based *H. pylori* therapies.

D.Y. Graham: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Significant; RedHIll Biopharma, Ltd.. F. Consultant/Advisory Board; Modest; RedHill Biopharma, Ltd.. K.G. Hulten:

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## W5.6 | European survey of *Helicobacter pylori* primary resistance to antibiotics - Evolution over the last 20 years

F. Mégraud[1]; D. Huang[2]; M. Hoebeke[2]; C. Alix[1]; L. Bénéjat[1]; P. Lehours[1]; **Y. GluPczynski**[2]; The *H. pylori* AST Working Group

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**Introduction**: Antibiotic resistance of *Helicobacter pylori* is the main cause of failure of most current eradication regimens. As antimicrobial susceptibility testing (AST) is not performed in all cases, it is important to have regular surveys to infer the treatments which can be used. For this purpose, European surveys were performed in 1998, 2008 and we report here the results of 2018.

**Material & Methods**: Centres were recruited on a voluntary basis, one for each small country (in the range of 10 million inhabitants) and several for larger countries. The request was to include 50 adult patients who had not received previous eradication treatment. Information collected included demographic, clinical, and endoscopic results as well as AST results (clarithromycin, levofloxacin, metronidazole, amoxicillin, tetracycline and rifampicin) performed by Etest or disk diffusion according to a standardized procedure. Control strains were also made available and a 10% random sample was sent to the coordinating centre at the end.

**Results**: The crude data show 1,246 *H. pylori* positive patients included in 24 centres from 19 countries (minimum: 20 cases per centre) The distribution with regard to age, gender, reason for consultation and endoscopic examination is in the range of what is usually observed for this type of patients. *H. pylori* resistance was present in 21.9% for clarithromycin, 16.6% for levofloxacin, and 38.5% for metronidazole; 30 strains were reported as resistant to amoxicillin (2.4%), 4 to tetracycline (0.3%) and 48 to rifampicin compounds (3.8%). These unusual resistance strains are now being controlled as well as a random sample of the other strains. The kit Amplidiag *H.pylori* (MobiDiag) will be used for clarithromycin and AST for the other antibiotics.

**Conclusion**: These results indicate a global and continuous rise in *H. pylori* primary resistance to clarithromycin but lower than in the previous decade (9.9% in 1998, 17.5% in 2008, and 21.9% in 2018), a slight increase to levofloxacin and a more important increase for metronidazole (from 33.1 to 38.5% since 2008).

**Acknowledgment**: The authors acknowledge the support of bioMérieux for providing Etests and Mobidiag for providing PCR kits.

## W5.7 | The activity of liposomal linolenic acid against *Helicobacter pylori* in vitro and its impact on human fecal microbiota

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**Background & Aims**: *Helicobacter pylori (H. pylori)* infection is associated with a variety of gastrointestinal diseases. The eradication rate of *H. pylori* has been reduced due to antibiotic resistance. Here, we focused on the activity of liposomal linolenic acid (LipoLLA) against *H. pylori* in vitro and its impact on human fecal bacteria.

**Methods**: The minimum inhibitory concentration (MIC) of LipoLLA against 30 *H. pylori* clinical strains were determined and in combination with amoxicillin, metronidazole, levofloxacin and clarithromycin. The concentration sterilization curves were performed at different pH or different time. The mechanism of LipoLLA against *H. pylori* was studied by detecting the leakage of glucose (GLU) and aspartate aminotransferase (AST). The effect of LipoLLA on human fecal bacteria was studied by high-throughput sequencing of fecal samples.

**Results**: The range of MIC of LipoLLA against 30 strains was 3.75-15 μg/mL. The combination effect showed synergistic or additive. The concentration sterilization curves were pH and time dependent. After treated by LipoLLA, GLU and AST were increased ($P < 0.05$). LipoLLA had no significant changes in the intestinal flora according to alpha diversity, species composition, Beta diversity, etc.

**Conclusions**: LipoLLA showed good anti-*H. pylori* effect. It destroyed the outer membrane barrier and caused the leakage of the bacterial contents, which helps other antibiotics increase antibacterial activity. LipoLLA had little effect on human fecal bacteria.

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# WORKSHOP W6 MICROBIOTA IN HEALTH AND DISEASE

## W6.1 | Functional microbiomics – standardized assessment of nutrition-microbiome-host interplay by targeted metabolomics

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**Introduction**: In recent years, microbiome research has dramatically reshaped our understanding of how microbes impact on (patho-)

physiological processes of the host. Metabolomics allows the investigation of microbial metabolic activities, providing the ideal technology to assess functional nutrition-microbiota-host crosstalk. Here, we present the newly developed MxP® Quant 500 kit-based assay for the standardized quantification of endogenous and microbiota-derived metabolites.

**Methods**: A set of 14 samples (NIST SRM 1950, 6 human plasma samples, 2 human serum samples, lipemic human plasma, mouse plasma, rat plasma, mouse liver, and human feces), 10 µl each, were analyzed by eight independent beta-testers using MxP® Quant 500 on Agilent 1290 Infinity UHPLC - SCIEX QTRAP® 5500. The assay covers 630 metabolites: 106 small molecules from 13 compound classes are analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS), hexoses and 523 lipids from 12 lipid classes by flow-injection analysis (FIA)-MS/MS. Met*IDQ*™ software was used for the entire automated workflow.

**Results**: Absolute quantitation was achieved with an excellent analytical accuracy and precision across all beta-testers using a seven-point calibration or a one-point calibration with stable-isotope labeled internal standards, which provides the basis for longitudinal robustness and inter-laboratory comparability. In addition to endogenous metabolites, a multitude of microbiota-derived metabolites were quantified in all matrices.

**Conclusion**: With its standardized workflow and beta-test proven longitudinal robustness, the MxP® Quant 500 is the ideal tool for large cohort, multi-center studies, enabling the investigation of functional nutrition-microbiome-host interplay for uncovering causal links to pathophysiological processes, disease development, and response to drug treatment.

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## W6.2 | Combining nucleic acid mimics and spectral imaging with fluorescence *in situ* hybridization for the analysis of the gastric micro-biogeography

**A. S. Azevedo**[1,2,3]; H. Teixeira[1]; R. Ferreira[2,3]; C. Figueiredo[2,3]; J. Wengel[4]; C. Almeida[1,5,6]; N. Azevedo[1]

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Nucleic acid mimics (NAMs)-based assays, such as locked nucleic acid/2′-O-methyl-RNA-fluorescence *in vivo* hybridization (LNA/2′OMe-FISH), have been developed for the identification and spatial location of *Helicobacter pylori* directly in the stomach. While *H. pylori* is considered the main gastric pathogen, there is a diverse range of stomach colonizers that may be associated with disease in the stomach.

In this work, giving the enhanced hybridization properties of NAMs, we intend to combine them with FISH and spectral imaging, in one technique. This technique, designated as NAM-CLASI-FISH, will allow the evaluation of the gastric micro-biogeography.

We have selected 8 fluorochromes with distinct spectral properties and 8 mouse gastric bacterial species. To control thermodynamic parameters, LNA/2′OMe probes coupled with the different fluorochromes were used. Universal Eubacteria LNA/2′OMe probe sequences were used to rank the species/fluorochromes. Mixed samples were analyzed by Leica TCS SP5 Confocal; a linear unmixing algorithm was applied to identify the fluorochromes present in each pixel of the image. Lastly, the procedure was validated using mixed bacterial populations to evaluate its potential for quantifying different targets in a sample.

A strong variation on the fluorescence intensities was found between species and between fluorochromes, which were balanced by matching “weaker” species with “stronger” fluorochromes and vice versa. Validation tests with different proportions of bacteria labelled with the different fluorochromes have shown the method ability to correctly distinguish the different relative proportions of bacteria. Future work will focus on imaging and unmixing of unknown gastric samples labeled with the fluorochromes tested.

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## W6.3 | Patients with small intestinal bacterial overgrowth (SIBO) have distinct microbiome characteristics including post *Helicobacter pylori* eradication treatment

**T. T. Perets**[1,2]; O. Ashorov[1]; D. Hamouda[1]; S. Ben Simon[3]; D. Boltin[4,2]; O. Koren[3]; R. Dickman[4,2]

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**Introduction**: Gastrointestinal (GI) microbial populations play an important role in maintaining normal GI function and preventing disorders. Dysbiotic flora may increase the likelihood of small intestinal bacterial overgrowth (SIBO), a syndrome associated with significant morbidity. We aimed to investigate the microbiota populations of patients with SIBO.

**Methods**: Patients with symptoms of SIBO, specifically abdominal bloating and gas were consecutively enrolled. All patients performed SIBO hydrogen breath test and stool was collected for microbiome analysis by sequencing of the 16S ribosomal RNA gene. A positive SIBO test was defined when hydrogen concentrations exceeded baseline measurements by 20 PPM.

**Results**: There were 55 patients of which 39 were females, mean age 53 ± 17 years, mean BMI 25 ± 4. Out of the 55 patients, 42 [76.4% (29 females)] had a positive SIBO test and 13 negative [23.6% (10 females)]. Importantly, patients with a negative SIBO had significantly more Methanobrevibacter-a strictly anaerobic genus of the Methanobacteriaceae ($q = 0.025$). Further evaluation revealed a subgroup of 7 [12.7%] patients (2 SIBO positive and 5 SIBO negative) who were treated previously (1st line) for *Helicobacter pylori* (*HP*) with interval of 24-36 months since treatment for *HP*. Microbiome analysis of these patients demonstrated significant decrease in their α-diversity ($q = 0.001$) compared to patients without previous *HP* therapy.

**Conclusions**: It is apparent that SIBO positive patients differ slightly from SIBO negative in their diversity of methane producing microbiome. Our results support previous observations regarding antibiotics altering GI microbiome taxa and function by showing that first line treatment antibiotic for *HP* eradication triggers dysbiosis.

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## W6.4 | The difference of gut microbiome in the stage of colorectal cancer and change of gut microbiome after surgery or chemotherapy

**J. Cho**[1]; D. Lee[1,2]; Y. Lee[2]; M. Seol[2]; Y. Kim[3]; W. Lee[4]; Y. Kim[4]; Y. Park[1]; C. Shin[1]; H. Yoon[1]; N. Kim[1]; S. Seol[5]

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**Background/Aim**: There has been few reports of gut microbiome change regarding to colorectal cancer (CRC) stages and posttreatment.

**Methods**: Fecal samples from Korean 42 patients with CRC stage I-IV were collected before and 6 months after treatment (surgery or chemotherapy). Sequencing was based on the 16S rRNA gene amplicon on the Illumina MiSeq platform.

**Result**: In the metagenomic analysis according to CRC stages, the relative abundance of *Facalibacterium* and *Streptococcus* was decreased in stage IV than in stage I-III, while the relative abundance of *Ruminococcaceae* was increased in stage IV than in stage I-III. After treatment, bacterial diversity was recovered at 6 months after surgery or chemotherapy compared to before treatment. The relative abundance of the phylum Proteobacteria was increased, while the phylum Bacteroidetes was decreased after treatment. Furthermore, the relative abundance of *Faecalibacterium*, *Acidobacteria* was increased, while *Bacteroides* and *Akkermansia* was decreased. Comparing between surgery and chemotherapy, the surgery group showed the less microbiota diversity than the chemotherapy group. In the surgery group, the level of genus such as *Bacteroides*, *Prevotella*, *Collinsella*, *Megamonas* and the level of family Enterobacteriaceae were observed highly, while *Fusobacterium* and *Ruminococcus* were decreased.

**Conclusion**: There are differences in the relative abundance of some of gut microbiome in the CRC stage IV compared to stage I-III. Together, microbial diversity was recovered at 6 months after surgery or chemotherapy compared to before CRC treatment. In terms of comparing between surgery and chemotherapy, we found the decrease of gut microbial diversity after surgery than chemotherapy.

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## W6.5 | Microbiota changes induced by microencapsulated sodium butyrate

**S. Facchin**[1]; N. Vitulo[2]; M. Calgaro[2]; A. Buda[3]; R. Chiara[4]; B. Perini[1]; G. Lorenzon[1]; C. Marinelli[1]; E. Savarino[1]

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**Introduction**: Inflammatory bowel disease (IBD) is characterized by severe inflammation of the small bowel and/or the colon. The Butyrate produced by anaerobic bacteria shown anti-inflammatory and regenerative properties. Limited data are available on butyrate effectiveness in patients with IBD due to the difficulties of proving an adequate concentration of butyrate in the colon.

**Aims & Methods**: We investigate the effect of a microencapsulated form of sodium Butyrate (MSB, Butyrose SILA, Noale, Italy) on the fecal microbiota of patients with IBD. In this prospective randomized-placebo-controlled study, 49 IBD patients, 19 CD, and 30 UC and 18 healthy volunteers were enrolled. After stratification by clinical assessment, colonoscopy, and fecal calprotectin (FC) levels, the patients were randomized to oral administration of MSB or placebo for 2 months. Before (T0) and after (T1) butyrate treatment, stool samples were collected for 16S rRNA analysis. Patients completed the quality of life questionnaire (QoL-IBDQ) on T = 0 and T = 1.

**Results**: MSB increased the bacteria able to produce short-chain fatty acids (SFCA); especially *Butyricicoccus* and *Subdoligranulum* were observed in CD patients whereas *Lachnospiraceae* in UC patients. Clinically, a 30% decrease of FC-levels were observed in 67% of CD Butyrate patients treated vs 33.3% in those with placebo-treated. Subjective improvement in QoL based on IBDQ was significantly observed especially in UC patients.

**Conclusion**: MSB supplementation showed an increase of SCFA bacteria stimulating growth with a mimicking prebiotic effect increasing the production of endogenous and physiological SCFAs with a marked improvement of QoL and reduction of the level of inflammatory markers

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## W6.6 | *Saccharomyces boulardii* CNCM I-745 as complementary treatment of *Helicobacter pylori* infection on gut microbiome

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*Rationale:* Conventional therapy for *H. pylori*(HP) infection includes the combination of antibiotics and a proton-pump inhibitor. Addition of probiotics as adjuvants for HP treatment can increase eradication rate and decrease treatment side-effects. Although many studies show the benefits of *S. boulardii* CNCM I-745 (SB) in the treatment of *H. pylori* infection, the mechanism by which those benefits are achieved are unknown. Here, we report clinical characteristics and fecal microbiota changes comparing conventional anti-HP therapy vs conventional therapy supplemented with SB. Patients and

**Methods**: A total of 74 patients were included in the current study; patients positive for *HP* (n = 63) were randomly assigned to 2 groups: 34 patients received conventional therapy and 29 antibiotic therapy plus 750 mg of SB for two-weeks. Eleven patients negative for HP were also studied. Patients provided 3 fecal samples: before initiating the treatment, immediately upon its completion and one month after completion. Patients were contacted every 72 hours during antibiotic therapy to inquire about side effects and compliance. 16S rRNA was amplified and sequenced on Illumina MiSeq. Bioinformatic analysis was performed using QIIME2.

**Results**: Patients that received SB had a lower frequency of gastrointestinal symptoms; higher number of diversity evenness ($P$ = 0.0156); higher abundance of *Enterobacteria*; and lower abundance of Bacteroides and Clostridia upon treatment completion and one-month later. Bacteroides and Clostridia have been previously implicated as antibiotic multi-resistant pro-inflammatory strains.

**Conclusion**: Addition of SB to treatment for HP infection induced a lower frequency of gastrointestinal symptoms that could be related to gut microbiota changes.

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## W6.7 | Efficacy and safety of new Lactobacilli mixture in patients with unconstipated irritable bowel syndrome: A randomized, double-blind, placebo-controlled trial

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**Background and Aim**: Increasing evidence showed that supplement of the specific bacteria appears to positive effects on irritable bowel syndrome (IBS). According to our previous animal models, multi-strain probiotics, including *Lactobacillus paracasei*, *L. salivarius* and *L. plantarum* have been shown potential utility in IBS. The objective of this study was whether these novel probiotics could provide improving abdominal symptom for patients with IBS without constipation.

**Methods**: Fifty Vietnamese patients with unconstipated IBS were randomly assigned to either the probiotics or placebo groups. During the intervention, subjects took the probiotics supplement named Food is Lactobacillus, once a day. Patients weekly recorded their subject global assessment (SGA) and assessed with visual analogue scale (VAS) during the 4-week study period. Patients with 2 points or more of SGA score or decrease of 30% VAS score were considered responders. Patients who weekly respond for more than 2 of the 4 weeks were considered overall responders.

**Results**: There was no significant difference in demographic characteristics between the two groups. Overall responder rates of improvement of symptoms were significantly higher in the probiotics group (80.8%) than the placebo groups (45.8%) ($P = 0.009$). The overall responder rates assessed by VAS score were also higher in the probiotics group (69.2%, 41.7%, $P = 0.048$). There were no adverse events for either group during the study period.

**Conclusions**: Our findings suggest that the new combination of Lactobacilli appears to be promising in the relief of abdominal symptoms in Vietnamese patients with diarrhea-predominant or mixed IBS.

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# POSTER ROUND 1.1: TREATMENT OF HELICOBACTER INFECTION

## P1.01 | First-line *H. pylori* eradication therapy in Europe: Results from 21,487 cases of the European Registry on *H. pylori* Management (Hp-EuReg)

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**Background**: The best approach for *Helicobacter pylori* management remains unclear. Audit processes are essential to ensure that clinical practice is aligned with best standards of care.

**Methods**: International multicenter prospective non-interventional registry starting in 2013 aimed to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists. All infected adult patients were systematically registered at AEG-REDCap e-CRF. *Variables included*: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Intention-to-treat and per-protocol analyses were performed. Data monitoring was performed to ensure the quality of the data.

**Results**: So far, 21,487 first-line prescriptions from 27 European countries have been evaluated. Average age was 49 years, 60% women, and 18% had peptic ulcer. Pre-treatment resistance rates were: 24% to clarithromycin, 34% metronidazole, and 14% both. Drug prescription and efficacy is shown in the table. Triple therapy with amoxicillin and clarithromycin was the most commonly prescribed(45%), achieving, overall, <80% eradication rate. Over 90% eradication was obtained only with 10-day bismuth quadruple therapies or 14-day concomitant treatment. Longer treatment duration, higher acid inhibition and compliance were associated with higher eradication rates in the multivariate analysis.

**Conclusions**: Triple therapies account for the majority of prescriptions, however, only quadruple therapies lasting at least ten days are able to achieve over 90% eradication rates.

| Treatment | N | % Use | ITT | mITT | PP |
|---|---|---|---|---|---|
| PPI + C+A | 8,374 | 39% | 68.4% | 84.2% | 84.7% |
| PPI + C+A+M | 4,156 | 19% | 86.1% | 90.0% | 90.5% |
| PPI + C+A+B | 1,525 | 7.1% | 78.6% | 92.8% | 93.1% |
| PPI + M+Tc+B s.c. | 1,520 | 7.1% | 82.9% | 94.7% | 95.3% |
| PPI + C+A+T seq | 1,166 | 5.5% | 76.9% | 91.3% | 91.9% |
| PPI + C+M | 1,043 | 4.9% | 70.0% | 81.1% | 81.5% |
| PPI + C+A+M seq | 608 | 2.8% | 74.8% | 81.0% | 83.2% |
| PPI + A+M | 560 | 2.6% | 65.8% | 85.4% | 85.5% |
| PPI + A+L | 404 | 1.9% | 76.6% | 81.4% | 81.8% |
| PPI + M+Tc+B | 188 | 1.3% | 77.6% | 93.1% | 93.7% |
| PPI + C+A+T | 172 | 0.9% | 83.6% | 94.9% | 96.1% |

ITT - intention to treat, PP - per-protocol, 95%CI - 95% confidence interval, PPI - proton pump inhibitor, Seq - sequential, C - clarithromycin, M - metronidazole, T - tinidazole, A - amoxicillin, L - levofloxacin, B - bismuth, Tc - tetracycline, s.c. - single capsule.

A.G. McNicholl: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Mayoly, Allergan, Takeda, MSD. F. Consultant/Advisory Board; Modest; Mayoly. O.P. Nyssen: None. D.S. Bordin: None. B. Tepes: None. A. Perez-Aisa: None. D. Vaira: None. M. Caldas: None. L. Bujanda: None. M. Castro-Fernandez: None. F. Lerang: None. M. Leja: None. L. Rodrigo: None. T. Rokkas: None. L. Kupcinskas: None. J. Perez-Lasala: None. L.V. Jonaitis: None. O. Shvets: None. A. Gasbarrini: None. H. Simsek: None. A.T.R. Axon: None. G.M. Buzas: None. J.C. Machado: None. Y. Niv: None. L. Boyanova: None. A. Goldis: None. V. Lamy: None. M. Katicic: None. K. Przytulski: None. C. Beglinger: None. M. Venerito: None. P. Bytzer: None. L.G. Capelle: None. T. Milosavljevic: None. L.I. Veijola: None. J. Molina-Infante: None. L. Vologhzanina: None. G. Fadeenko: None. I. Ariño: None. G. Fiorini: None. M. Ramas: None. M.G. Donday: None. F. Megraud: None. C. O'Morain: None. J.P. Gisbert: Other; Modest; Dr. Gisbert has served as speaker, consultant and advisory member for or has received research funding from Casen Recordati, Mayoly, Allergan, Advia, Diasorin.

## P1.02 | Efficacy of first-line regimens in Spain: Results from the European Registry on *H. pylori* management (Hp-EuReg)

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**Introduction**: Updated data concerning Spain is needed to design the best strategy to treat *Helicobacter pylori (H. pylori)* infection.

**Aim**: To analyse the efficacy of the most commonly prescribed first-line therapies in Spain.

**Methods**: Observational, prospective study embracing 48 Spanish hospitals, included in the Hp-EuReg project. Inclusion period extended from February 2013 to January 2018. A multivariate analysis was performed considering the efficacy and the type of proton pump inhibitor (PPI) dose, treatment duration, compliance, gender and penicillin allergy.

**Results**: 8,581 patients naïve to *H. pylori* treatment were included, 61% of them being women and 4% allergic to penicillin. Median age was 51 years. Patients non-allergic to penicillin mostly received non-bismuth quadruple concomitant therapy (Q-NBCT, 43%), triple therapy containing clarithromycin and amoxicillin (T-CA, 35%), bismuth quadruple therapy adding clarithromycin and amoxicillin (Q-BCA, 9%) and the three-in-one single capsule (Q-SINGLE, 8%). Patients allergic to penicillin mostly received a triple therapy containing clarithromycin and metronidazole (T-CM, 42%) and Q-SINGLE treatment (32%). All therapies included a PPI. The efficacy analyzed on a modified ITT (mITT) and PP basis is shown in Table 1. Compliance was the variable most closely associated with efficacy ($P < 0.05$).

**Conclusions**: In first-line, the best efficacy results were obtained with Q-NBCT and Q-BCA (both during 14 days), and with Q-SINGLE (10 days), this last treatment both in allergic and in non-allergic to penicillin patients.

| | | mITT efficacy | | PP efficacy | |
|---|---|---|---|---|---|
| | Duration (days) | N included | mITT (95% C.I.) | N included | PP (95% C.I.) |
| *No penicillin allergy* | | | | | |
| Q-NBCTN = 3,504 | 10 | 2,130 | 86% (85-88%) | 2,031 | 89% (87-90%) |
| | 14 | 1,288 | 91% (89-92%) | 1,237 | 92% (91-94%) |
| T-CAN = 2,898 | 10 | 1,965 | 82% (81-84%) | 1,869 | 86% (84-87%) |
| | 14 | 742 | 81% (77-83%) | 675 | 87% (85-90%) |
| Q-BCAN = 722 | 14 | 697 | 91% (89-93%) | 670 | 94% (92-96%) |
| Q-SINGLEN = 652 | 10 | 593 | 93% (91-95%) | 574 | 95% (93-97%) |
| Q-NBSTN = 232 | 10 | 220 | 82% (76-87%) | 191 | 84% (78-89%) |
| *Penicillin allergy* | | | | | |
| T-CMN = 113 | 10 | 79 | 61% (49-72%) | 77 | 62% (51-73%) |
| Q-SINGLEN = 85 | 10 | 78 | 91% (82-96%) | 74 | 93% (85-98%) |
| Q-BTMN = 56 | 10 | 41 | 85% (71-94%) | 39 | 87% (73-96%) |

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## P1.03 | Pan-European Registry on *H. pylori* Management (Hp-EuReg): Experience with single capsule bismuth quadruple therapy in 2,326 patients

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**Background**: Bismuth-quadruple therapy with a PPI, bismuth salts, tetracycline and metronidazole has resurfaced in Europe thanks to a new single-capsule formulation (Pylera®).

**Methods**: Our aim was to evaluate the efficacy and safety of the single-capsule bismuth-quadruple therapy (Pylera®) in the European Registry on *Helicobacter pylori* management. Patients were systematically registered at an e-CRF by AEG-REDCap. *Variables included*: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Intention-to-treat and per-protocol analyses were performed. Data monitoring was performed to ensure the quality of the data.

**Results**: So far, 30,394 patients have been included. Of these, 2,326 valid patients treated with single-capsule bismuth-quadruple therapy have been evaluated. 1,900 (81.7%) were prescribed following the technical-sheet (10 days, 3 capsules q.i.d.), the remaining where excluded. Average age was 52 years, 64% women, and 13% had peptic ulcer. Table summarizes results. The majority of cases (63%) were naïve. PPI type or dose did not influence eradication rate. 33% of cases suffered from adverse events (severe in 3%, and only 1% withdrew treatment due to adverse events). Only two serious adverse events were reported: hospitalization for diarrhea, and an allergic reaction treated with anti-histamine drugs, both solved without complications.

**Conclusions**: Treatment with single-capsule bismuth-quadruple therapy (Pylera®)achieves *H. pylori* eradication in approximately 90% of patients by intention-to-treat in clinical practice, both in first- and second-line, with a favorable safety profile.

| | Frequency | Percent | mITT | PP |
|---|---|---|---|---|
| Naive (no previous treatment) | 1,195 | 63% | 92% | 95% |
| 2nd | 412 | 22% | 87% | 90% |
| 3rd | 220 | 12% | 84% | 85% |

mITT: Modified intention-to-treat; PP: per-protocol.

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## P1.04 | Pan-European Registry on *H. pylori* Management (Hp-EuReg): First-line treatment use and efficacy trends in 2013-2018

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**Background**: The impact of consensus, prescription choices and efficacy trends on clinical practice over time has not been studied in depth.

**Methods**: International multicenter prospective non-interventional registry starting in 2013 aimed to evaluate the decisions and outcomes of *H. pylori* management by European gastroenterologists. All infected adult patients were systematically registered at AEG-REDCap e-CRF. *Variables included*: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Intention-to-treat analyses were performed. Data monitoring was performed to ensure the quality of the data.

**Results**: So far 25,256 patients from 27 European countries have been included, 19,754 (77%) were naïve empirical prescriptions. Although, overall, the most common prescribed treatments in the 2013-18 period were triple therapies, a shift in antibiotic regimens was identified. Triple therapies decreased from over 50% of prescription in 2013/14 to less than 25% in 2017/18 while Pylera® has increased from 0-1% (2014/2015) to 25% (2018). Full description of most common treatments is shown in Table 1. Regarding the efficacy of each treatment no trend has been identified (data now shown), however there has been a 5% overall improve in first-line efficacy (Table 1).

**Conclusions**: European gastroenterological practice is constantly adapting to the newest published evidence and recommendations, and although this shift is delayed and slow, it improves clinical practice outcomes.

| | Year of visit | | | | | |
|---|---|---|---|---|---|---|
| | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
| Triple C+M | 116 | 271 | 317 | 262 | 41 | 8 |
| Triple C+A | 1,541 | 2,192 | 1,478 | 1,127 | 1,002 | 196 |
| Triple A+M | 164 | 181 | 75 | 31 | 19 | 1 |
| Triple A+L | 76 | 104 | 117 | 75 | 11 | 1 |
| Sequential C+A+T | 231 | 263 | 236 | 61 | 302 | 69 |
| Sequential C+A+M | 354 | 156 | 54 | 21 | 6 | 1 |
| Quadruple M+Tc+B | 70 | 83 | 12 | 2 | 6 | 1 |
| Quadruple C+A+T | 6 | 31 | 91 | 34 | 8 | 7 |
| Quadruple C+A+M | 753 | 910 | 943 | 786 | 663 | 65 |
| Quadruple C+A+B | 42 | 83 | 195 | 766 | 408 | 148 |
| Pylera | 1 | 1 | 21 | 502 | 788 | 183 |
| Other | 136 | 189 | 239 | 200 | 174 | 47 |
| mITT | 85.8% | 86.3% | 86.2% | 88.3% | 89.7% | 90.4% |

A.G. McNicholl: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Mayoly, Allergan, Takeda, MSD. F. Consultant/Advisory Board; Modest; Mayoly. O.P. Nyssen: None. D.S. Bordin: None. B. Tepes: None. A. Perez-Aisa: None. D. Vaira: None. M. Caldas: None. L. Bujanda: None. F. Lerang: None. M. Leja: None. T. Rokkas: None. L. Kupcinskas: None. L.V. Jonaitis: None. O. Shvets: None. A. Gasbarrini: None. G.M. Buzas: None. J.C. Machado: None. Y. Niv: None. L. Boyanova: None. V. Lamy: None. M. Venerito: None. M. Katicic: None. L.G. Capelle: None. T. Milosavljevic: None. G. Fiorini: None. M. Ramas: None. M.G.

Donday: None. F. Megraud: None. C. O'Morain: None. J.P. Gisbert: Other; Modest; Dr. Gisbert has served as speaker, consultant and advisory member for or has received research funding from Casen Recordati, Mayoly, Allergan, Advia, Diasorin.

## P1.05 | Efficacy of second-line regimens in SPain: Results from the EuroPean Registry on *H. Pylori* management (HP-EuReg)

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**Introduction**: The best second-line regimen against *Helicobacter pylori (H. pylori)* must be established locally to reach high eradication rates.

**Aim**: To evaluate the efficacy of the most frequently prescribed second-line treatments in Spain.

**Methods**: Observational and prospective study carried out in 48 Spanish hospitals, included in the 'Hp-EuReg' project. Patients were registered from February 2013 to January 2018. A multivariate analysis was performed considering the efficacy and the type of proton pump inhibitor (PPI) dose used, duration, compliance, gender and penicillin allergy.

**Results**: 1,869 patients received a second-line therapy: 67% were women and 6% had penicillin allergy. 93% had previously received a clarithromycin-containing regimen. Non-allergic to penicillin patients mostly received: triple therapy comprising levofloxacin and amoxicillin (T-LA, 45%), quadruple therapy adding bismuth to the previous therapy (Q-BLA, 24%), three-in-one single capsule (Q-SINGLE, 14%) and triple therapy using moxifloxacin and amoxicillin (T-MXA, 5%). All therapies comprised a PPI. Efficacy was analyzed on a modified ITT (mITT) and PP basis. Results are shown in Table 1. Compliance was the variable most closely associated with efficacy ($P < 0.05$).

**Conclusions**: In second-line, around 90% of efficacy was obtained with Q-SINGLE (10 days) and Q-BLA (14 days) in non-allergic to penicillin patients.

**TABLE 1.** Efficacy with the treatments more frequently prescribed in second line

| | | mITT efficacy | | PP efficacy | |
|---|---|---|---|---|---|
| | Duration (days) | N included | mITT (95% C.I.) | N included | PP (95% C.I.) |
| *No penicillin allergy* | | | | | |
| T-LAN = 792 | 10 | 586 | 71% (67-75%) | 564 | 73% (69-76%) |
| | 14 | 190 | 86% (81-91%) | 179 | 92% (87-95%) |
| Q-BLAN = 413 | 14 | 400 | 88% (84-91%) | 375 | 91% (88-94%) |
| Q-SINGLEN = 245 | 10 | 223 | 89% (84-93%) | 212 | 93% (89-96%) |
| T-MXAN = 92 | 14 | 69 | 86% (75-93%) | 66 | 89% (79-96%) |
| *Penicillin allergy* | | | | | |
| T-CLN = 30 | 10 | 24 | 71% (49-87%) | 21 | 76% (53-92%) |
| Q-BTMN = 30 | 10 | 18 | 72% (47-90%) | 18 | 72% (47-90%) |
| Q-SINGLEN = 85 | 10 | 23 | 78% (56-93%) | 21 | 86% (64-97%) |

T-CL: triple therapy (PPI, clarithromycin, levofloxacin). Q-BTM: quadruple therapy (PPI, bismuth, tetracycline and metronidazole).

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## P1.06 | OPtimum second-line regimens for *Helicobacter Pylori* eradication: Interim results of an ongoing Cochrane systematic revieW

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**Background**: *H. pylori* first-line eradication treatment frequently fails, mainly due to antibiotic resistance.

**Aims**: To evaluate the effects of second-line treatments on *H. pylori* eradication through systematic review of randomised controlled trials (RCTs).

**Methods**: Bibliographical searches were performed up to January 2019. Selection: RCTs comparing the efficacy of at least two different second-line treatments. The previous failed regimen should have contained at least two antibiotics. Exclusions: Studies assessing a second-line therapy based on bacterial antibiotic susceptibility or the use of any type of adjuvant. Efficacy: determined by intention-to-treat analysis. Results were combined by meta-analysing risk differences (RD) stratified by first-line therapy. The Cochrane risk-of-bias tool was used to assess risk of bias.

**Results**: 41 RCTs were included, and 39 comparisons of second-line different antibiotic combinations were analysed. Two comparisons improved eradication rates after failure of standard triple therapy (Table 1).

**Conclusion**: After a first-line standard triple therapy (PPI, clarithromycin, amoxicillin) failure, triple therapy with a PPI, amoxicillin and metronidazole showed higher eradication rates than the combination of a PPI, amoxicillin and levofloxacin. Standard quadruple therapy during 14 days, as compared to 7 days, showed better results. These preliminary results need to be read cautiously due to the limited number of studies and their high risk of bias.

**TABLE 1.** Meta-analyses performed for the 9 second-line therapy comparisons after failure of a first-line standard triple therapy

| Experimental arm | Control arm | RD [95%CI] | N° of studies[1] |
|---|---|---|---|
| PPI + A + M | PPI + A | 0.01 [-0.23, 0.22] | 3 |
| PPI + A + M | PPI + A + L | **0.21 [0.09, 0.33]*a** | **2** |
| PPI + A + M[a] | PPI + A + M[b] | 0.03 [-0.08, 0.14] | 3 |
| E + A + Mox | E + M + Tc + TDB | 0.03 [-0.16, 0.09] | 3 |
| O + Bs + A + M | O + A + Tc + Bs | 0.12 [-0.01, 0.24] | 2 |
| PPI + M + Tc + Bs (14 days) | PPI + M + Tc + Bs (7 days) | **0.16 [0.07, 0.26]*b** | **3** |
| PPI + L + Azit | PPI + M + Tc + Bs | -0.08 [-0.40, 0.24] | 2 |
| PPI + L + T | PPI + M + Tc + Bs | 0.04 [-0.36, 0.45] | 2 |
| PPI + A + L | PPI + M + Tc + Bs | 0.04 [-0.27, 0.36] | 3 |

[1]Number of studies included in each comparison; RD-risk difference; CI-confidence interval; PPI-proton pomp inhibitor; A-amoxicillin; Azit- azithromycin; Bs-bismuth salts; C-clarithromycin; E-esomeprazole; L-levofloxacin; Mox-moxifloxacin; M-metronidazole; Ma-metronidazole 750 mg; Mb-metronidazole 500 mg; O-omeprazole; T-tinidazole; Tc-tetracycline; TDB-tripotassium dicitrate bismuthate; * significance level $P \leq 0.05$; [a]2 studies, $I2$=0%; High risk of bias; [b]3 studies, $I2$=53%; High risk of bias

O. P. Nyssen: None. A. C. Marin: None. A. G. McNicholl: None. V. Savarino: None. X. Calvet: None. G. I Leontiadis: None. L. Fischbach: None. Y. Yuan: None. A. Crespo Cañizares: None. G. Escobar Aguilar: None. E. Fernández Martínez: None. E. García García: None. S. Hernandez Iglesias: None. C. Martín-Saborido: None. C. Sánchez Martín: None. D. Varillas Delgado: None. J. Lopez-Alcalde: None. J. P. Gisbert: None.

## P1.07 | Effects of *Helicobacter pylori* eradication for recurrent neoplasia prevention after endoscopic submucosal dissection of gastric adenoma

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**Background and Aims**: After endoscopic submucosal dissection (ESD) of gastric adenoma, whether *Helicobacter pylori* eradication reduces the occurrence of metachronous gastric lesions (MGL) is still debatable. The aim of this study was to evaluate the effects of *H. pylori* eradication on the development of MGL after ESD of gastric adenoma.

**Methods**: A total of 244 patients with gastric adenoma treated by ESD were enrolled. Annual endoscopic surveillance was executed after ESD. Patients group were classified into the two group according to *H. pylori* eradication; eradicated group (n = 143) and not eradicated group (n = 101).

**Results**: At 28 months' median follow-up, MGL had developed in 36 patients (14.8%), including 31 with adenomas and 5 with cancers. Although the rate of MGL was lower in the eradicated group than not eradicated group (12.6% [18/143] vs 17.8% [18/101]), it was not statistically significant ($P = 0.256$). In patients ≥ 60 years of age, the rate of MGL was significantly lower in the eradicated group than in the not eradicated group (12.1% vs 23.9%, $P = 0.042$). A multivariable analysis of the old age subgroup, risk factors for MGL included persistent *H. pylori* infection.

**Conclusions**: Although not applicable to all ages, *H. pylori* eradication might prevent the development of MGL after ESD of gastric adenoma in patients ≥ 60 years of age.

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## P1.08 | Clarithromycin resistance test could improve the eradication rate of *H. pylori*

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**Aim**: This study is to evaluate the effectiveness of treatment with CAM resistance test.

**Methods**: We performed PCR-based sequencing to detect CAM resistance-associated mutations using biopsy specimen that were positive in the CLO test. Patients who did not have CAM resistance mutation were treated with standard triple therapy for 7 days. And patients with CAM resistance mutation were treated with Bismuth contained quadruple therapy for 7 days. Eradication was confirmed using the CLO test or 13C-labelled urea breath test.

**Results**: A total 273 patients completed the evaluation of the success of eradication. 172 of 273 (62.5%) patients did not have any clarithromycin resistance mutation, 101 patients had clarithromycin resistance mutation. Of the 172 patients without mutation, 170 patients were treated with conventional triple therapy and 2 patient was treated with bismuth quadruple therapy because of side effect (headache) of fist line therapy. Except twelve patients treated with conventional triple therapy, all patients without mutation were successful in eradication. And 101 patients with mutation, patients were treated with bismuth quadruple therapy and all but three of them were eradicated. Overall intention-to-treat eradication rates were 94.5%.

**Conclusion**: As compared with 75% to 80% success rate of conventional treatment of eradication, the 94.5% success rate with CAM resistance test is remarkable. Therefore, the patient-tailored treatment strategy through the CAM resistance test is promising.

J. Jung: None. J. Kwon: None. E. Kim: None.

## P1.10 | Single-capsule bismuth-quadruple therapy: 3 or 4 times daily? Spanish Data from the European Registry on *H. pylori* Management (Hp-EuReg)

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**Background**: Single-capsule bismuth-quadruple therapy with a PPI, bismuth, tetracycline and metronidazole (Pylera®) regimen is dosed as 3 capsules four times daily (3/qid). This scheme may not be adequate for late-dinner Spanish habit. Therefore, some physicians prescribe the treatment as a 4 capsules three times daily (4/tid). Our

aim was to evaluate the efficacy and safety of tPylera® 4/tid in the European Registry on *H. pylori* management in Spain.

**Methods**: Patients were registered at an e-CRF by AEG-REDCap. Variables included: Patient's demographics, previous eradication attempts, prescribed treatment, adverse events, and outcomes. Intention-to-treat and per-protocol analyses were performed. Data monitoring was performed to ensure the quality of the data. Descriptive statistics was performed using SPSS 21.

**Results**: Of the 2,326 valid Spanish patients treated with single-capsule bismuth-quadruple therapy, 1,140 (74%) were prescribed 3/qid, and 403 4/tid. Average age was 48 years, 63% were women, and 11% had peptic ulcer. The majority of cases (72%) were naïve. PPI type or dose did not influence eradication rates. Both treatments provided equivalent compliance, adverse events and eradication rates (table). Only one case suffered a serious adverse event (C. difficile infection) in the 3/qid group.

| | | Adverse | Intention-to-treat | | | | Per-protocol | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Pylera | Compliance (%) | Events (%) | Overall (%) | Naive (%) | Second (%) | Third (%) | Overall (%) | Naive (%) | Second (%) | Third (%) |
| 4/tid | 97 | 22 | 85 | 95 | 92 | 86 | 93 | 96 | 94 | 92 |
| 3/qid | 98 | 24 | 86 | 93 | 83 | 84 | 90 | 95 | 87 | 86 |

**Conclusions**: Prescription of single-capsule bismuth-quadruple therapy as a 4 capsules three times daily seems to achieves at least the same compliance, tolerance and efficacy than the 3 capsules four times daily schedule proposed in the technical sheet.

## P1.11 | Ultimate eradication rate of *Helicobacter pylori* in Korea: A single center experience

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**Background and Aims**: Resistance rates of *Helicobacter pylori* to clarithromycin, metronidazole, and quinolone are rapidly increased in South Korea. The aim of this prospective study was to evaluate the ultimate eradication rate of *H. pylori* after first, second, or third-line therapy in Korea.

**Methods**: 1496 patients with *H. pylori* was treated with proton pump inhibitor (PPI)-based triple therapy or concomitant therapy. In case of treatment failure or recurrence, Concomitant therapy or bismuth-based quadruple therapy was randomly given. When the second-line treatment failed or *H. pylori* recurred, the unused Levofloxacin based triple therapy was used as a third-line treatment.

**Results**: Among 1496 patients (intention-to treat [ITT]), 1144 (76.5%, per-protocol [PP]) completely followed our treatment. The ITT and PP rates of Fist line treatment were 55% and 71.9%. After second line, they reached 74.3% (ITT) and 97.1% (PP). The "final" eradication rate up to third line treatment were 75.8% (1134/1496) and 99.1% (1134/1144), respectively

**Conclusion**: Despite the high antibiotics resistance, the ultimate eradication rate of *Helicobacter pylori* in Korea was high, 99.1%. However, high rate of refusal of further treatment and follow-up loss made ITT eradication rate low. Proper strategy to improve the treatment adherence is needed.

M. Lee: None. G. Kim: None. B. Lee: None. E. Park: None. G. Song: None.

## P1.12 | The efficacy of Modified bismuth quadruple therapy for *Helicobacter pylori* infection in Korea. A single arm prospective observational study

**J. Choe**; S. Jung; S. Kim; J. Hyun; Y. Jung; J. Koo; H. Yim; S. Lee

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**Background**: Recently, we reported that modified bismuth quadruple therapy in which tetracycline was replaced by amoxicillin(PAM-B therapy) showed excellent clinical results in Korea. Further prospective longitudinal analysis with larger number was performed in our hospital. The aim of this study was to evaluate the effectiveness of a first line 14-day PAM-B therapy and investigate the optimal rescue treatment for the first-line treatment failure.

**Method**: A prospective observational study of *H. pylori* eradication was conducted in a single institute. A total of 324 treatment-naïve patients with active *H. pylori* infections, who were positive for *H. pylori* between April 2016 and January 2019, were included for analysis. All enrolled patients were treated with 14-day PAM-B therapy[rabeprazole 20 mg, amoxicillin 1 g, metronidazole 750 mg, and tripotassium dicitrato bismuthate 600 mg (elemental bismuth 240 mg) twice daily]. Six weeks after treatment, *H. pylori* eradication was assessed.

**Result**: Among the 324 participants, 30 patients were lost to follow-up and 9 patients consumed less than 80% of prescribed medication. So, the overall eradication rates by ITT, modified ITT and PP analyses were 83.0% (n = 269/324), 93.6% (n = 279/298) and 94.4% (n = 269/285). In 16 patients of treatment failure despite of good compliance, 11 patient were agreed to treat with 2nd line treatment with conventional bismuth-containing quadruple therapy. Among

them, eradication rate was 88.9%(n = 8/9) except 2 follow up loss patients.

**Conclusion**: PAM-B therapy was highly effective as a first line therapy for *H. pylori* eradication. Conventional bismuth quadruple therapy is thought to be sufficient as a rescue therapy.

J. Choe: None. S. Jung: None. S. Kim: None. J. Hyun: None. Y. Jung: None. J. Koo: None. H. Yim: None. S. Lee: None.

## P1.13 | Effectiveness and safety of furazolidone-containing quadruple regimens in patients with *Helicobacter pylori* infection: A real-world practice patterns in a developing country

**C. Song**; Y. Xie; Y. Zhu; X. Shu; N. Lu

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**Background & Aims**: The eradication rate of *Helicobacter pylori* (*H. pylori*) has decreased largely because of the antibiotic resistance. We aimed to evaluate the effectiveness and safety of furazolidone-containing quadruple regimens for *H. pylori* eradication.

**Methods**: This was an observational study of furazolidone-containing quadruple regimens for *H. pylori*infection in real-world settings. Data sets were collected from the medical records and telephone interviews of patients referred to a specialist clinic for suspected *H. pylori* reinfection from 1 January 2015 to 1 January 2018 at the First Affiliated Hospital of Nanchang University. Main outcome measures were the eradication rate and adverse reactions during medication.

**Results**: Among 584 patients with *H. pylori*infection that met the inclusion criteria, 561 (96.1%) were treated for the first time, 19 (3.3%) had one and 4 (0.5%) had two or more prior to furazolidone-containing quadruple regimens. The eradication rates for 10-d and 14-d regimens were 93.7% (95% CI: 91.5%-95.9%) vs 98.2% (95% CI: 95.6%-99.3%), respectively ($P$ = 0.098). Adverse drug reactions occurred in 8.2% (48/584) with abdominal discomfort being the most common symptom. Overall adverse events with 10-d regimens were lower than 14-d regimens (6.1% vs 17.4%, $P$ < 0.001). Logistic regression analysis indicated that poor adherence [(adjusted odds ratio (AOR) = 46.5, 95% CI: 9.7-222.4)] were correlated with failed eradication. Adverse drug reactions during medication were related to smoking and tobacco status, alcohol intake history, regimens combined with tetracycline, and poor adherence (all $P$ < 0.05).

**Conclusions**: Furazolidone-containing quadruple regimens proved both safe and highly effective in a real-world setting.

C. Song: None. Y. Xie: None. Y. Zhu: None. X. Shu: None. N. Lu: None.

## P1.14 | Comparative effect of Proton-pump Inhibitors on the Success of Quadruple Therapy for *Helicobacter pylori* Infection

**D. Boltin**[1]; Z. Levi[1]; R. Gingold-Belfer[1]; H. Schmilovitz-Weiss[1]; T. Shochat[1]; R. Dickman[1]; Y. Niv[1]; S. Birkenfeld[2]; I. Dotan[1]

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**Background**: Suppression of gastric acid secretion with proton-pump inhibitors (PPIs) is an integral part of treatment of *H. pylori* infection. Esomeprazole has been shown to be superior to other PPIs when used in the context of triple therapy, however comparative data for PPI efficacy in quadruple therapy are lacking. Current guidelines recommend *H. pylori* eradication with quadruple therapy in areas with high clarithromycin resistance. The aim of this study was to determine whether esomeprazole is more effective than other PPIs in the context of quadruple therapy for *H. pylori* eradication.

**Methods**: We retrospectively identified 25-60 year-old subjects with a positive $^{13}$C-urea breath test and no prior laboratory or endoscopic test for *H. pylori* infection. Pharmacy dispensation data were retrieved.

**Results**: A total of 7896 subjects including 2856 (36.2%) males, aged 40.4 ± 10.6 years, were identified. 78.1% received omeprazole, 20.1% received lansoprazole, 1.5% received esomeprazole and 0.34% received pantoprazole together with antibiotics for *H. pylori* eradication. Esomeprazole was associated with a greater proportion of successful eradication (85.0% vs 77.5%, esomeprazole *vs* omeprazole, OR 1.64; 95%CI 0.99-2.72; $P$ = 0.05). A non-significant trend favored esomeprazole over omeprazole among subjects receiving quadruple therapy (90.0% *vs* 82.0%, respectively, OR 1.98; 95%CI 0.68-5.72; $P$ = 0.16). Independent predictors of treatment success included older age and quadruple therapy.

**Conclusion**: Esomeprazole is more beneficial than other PPIs for *H. pylori* eradication. Studies with larger subgroups are necessary to confirm our findings among subjects receiving quadruple therapy.

D. Boltin: None. Z. Levi: None. R. Gingold-Belfer: None. H. Schmilovitz-Weiss: None. T. Shochat: None. R. Dickman: None. Y. Niv: None. S. Birkenfeld: None. I. Dotan: None.

## P1.15 | Antimicrobial susceptibility of *Helicobacter suis*, a zoonotic agent mainly associated with pigs and non-human primates

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*Helicobacter suis* is mainly associated with pigs and non-human primates, but the porcine strains can also cause gastric disease in

humans. Due to its very fastidious growth characteristics, few data are available on antimicrobial susceptibility of this agent.

Therefore, a combined agar and broth dilution method was used to analyze the activity of 15 antimicrobial agents against 20 and 15 *H. suis* isolates obtained from pigs and macaques, respectively. After 48 hours microaerobic incubation, minimal inhibitory concentrations (MICs) were determined by software-assisted calculation of bacterial growth as determined by quantitative real-time PCR.

A monomodal distribution of MICs was seen for β-lactam antibiotics, macrolides, gentamicin, neomycin, doxycycline, metronidazole, and rifampicin. A bimodal distribution was demonstrated in 2 porcine isolates for fluoroquinolones, in 1 primate isolate for spectinomycin, in 1 porcine and 2 macaque isolates for lincomycin, and in 1 porcine isolate for tetracycline. Remarkably, MICs of ampicillin were higher for porcine *H. suis* isolates compared to macaque isolates. Single nucleotide polymorphisms (SNPs) were present in the *gyrA* gene of *H. suis* isolates with acquired resistance to fluoroquinolones, in the *30S ribosomal protein* genes of tetracycline or spectinomycin resistant strains and in *penicillin binding protein* genes of porcine isolates with high MICs of ampicillin.

This study demonstrates that acquired resistance occurs in *H. suis* isolates and indicates that porcine isolates are less susceptibility to aminobenzyl penicillins. This may be important for treatment of *H. suis* infections in human patients.

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## P1.16 | Efficacy of flavodoxin inhibitors against *Helicobacter pylori* drug-resistant clinical strains and in Hp-infected mice

**J. Sancho**[1]; S. Salillas[1]; M. Alías[2]; V. Michel[3]; A. Mahía[4]; A. Lucía[1]; L. Rodrigues[1]; J. Bueno[1]; J. J. Galano-Frutos[1]; H. de Reuse[3]; A. Velazquez-Campoy[1]; J. A. Carrodeguas[1]; C. Sostres[1]; J. Castillo[1]; J. A. Aínsa[1]; M. D. Díaz de Villegas[1]; Á. Lanas[1]; E. Touati[1]

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Eradication of *Helicobacter pylori* (Hp) infection, based on the combination of different antimicrobials, is being challenged by increasing antimicrobial resistance. To contribute to Hp-specific eradication, we have developed a novel family of Hp-specific antimicrobials, and have determined their efficacy against resistant clinical isolates and in the mouse model of Hp infection. We have designed, synthesized and tested redox variants of two families of compounds (containing nitroethylene or 7-nitrobenzoxadiazole) that inhibit the activity of flavodoxin, an essential Hp protein. Derivatives of nitroethylene show similar decreased cytotoxicity and antimicrobial activity and do not constitute a significant improvement from their parent compound. In contrast, derivatives of 7-nitrobenzoxadiazole display largely increased therapeutic indexes against several reference Hp strains. These inhibitors, which carry reduced forms of the nitro group and/or oxidized forms of the sulphur atom, are effective against metronidazole-, clarithromycin- and rifampicin-resistant clinical isolates of Hp. Besides, their toxicity for mice after oral administration is greatly reduced compared to that of the lead compound. When given individually at single daily doses for 8 days in a mice model of Hp infection, they reduced significantly the Hp gastric colonization rates and were able to eradicate the infection in up to 60% of the mice.

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## P1.17 | Comparison of the efficacy of vonoprazan-based first-line and second-line eradication therapy for *Helicobacter pylori* infection between 2015 and 2018

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**Background/Aim**: Vonoprazan (VPZ), a potassium-competitive acid blocker (P-CAB), has strong acid-inhibitory effects and has been used for the eradication of *H. pylori* since February 2015. VPZ-based eradication therapy has achieved higher eradication rate comparing with PPIs. The aim of this study was to investigate whether the efficacy of eradication therapy using VPZ remains high or reduced.

**Methods**: Patients who received eradication therapy in Mutsu General Hospital between February 2015 ~ January 2016 (initial period) and February 2018 ~ January 2019 (current period) were studied retrospectively. As the first-line therapy, patients infected with *H. pylori*administered VPZ (20 mg; bid) with amoxicillin (AMOX: 750 mg; bid) and clarithromycin (CAM: 200 mg; bid) for 7 days. Patients who failed first-line therapy administered metronidazole (MNZ) instead of CAM as the second-line therapy. 6-10 weeks after finishing the treatment, results of eradication therapy was assessed by either stool antigen test or $^{13}$C-UBT, which was used at the initial diagnosis of *H. pylori* infection.

**Results**: A total of 323 patients who received first-line and/or second-line eradication therapy were studied. All the patients completed the regimens without major side effects. The eradication rate of first-line was 92.4% (73/79; 95% CI: 86.6-98.2%) and 92.4% (207/224; 95% CI: 88.9-95.9%) during the current period, respectively. On the other hand, eradication rate of second-line therapies

was 100% (5/5) during the initial period and 93.3% (14/15; 95% CI: 79.0-107.6%) during the current period.

**Conclusions**: *H. pylori* eradication treatments using VPZ have been safe and effective since the introduction of VPZ.

S. Nakagawa: None. T. Shimoyama: None. D. Chinda: None. C. Iino: None. S. Fukuda: None. W. Onodera: None.

## P1.18 | In vitro activity of a new synthesized silver ultra-nanoclusters (SUNc) against *Helicobacter pylori*

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The infectious diseases are still one of the most important current challenges. The success of the antibiotic therapy is limited by the significant increase of the antibiotic resistance. *Helicobacter pylori* infection is difficult to manage and the use of new therapeutic approaches is needed. It has been widely demonstrated that silver nanoparticles have a strong activity against Gram-positive and Gram-negative bacteria, as well as viruses and fungi. The aim of this study was to evaluate the antimicrobial activity of a new synthesized (EP-18181873) silver ultra-nanoclusters (SUNc) formulation against *Helicobacter pylori*. SUNc was tested vs eight clinical *Helicobacter pylori* isolates with a different antibiotic susceptibility pattern and one reference strain (ATCC 43504), using the broth microdilution methodology. Furthermore, the time killing assay was performed on the *Helicobacter pylori* ATCC 43504, at 24 and 48 hours of incubation. The inhibitory concentrations of SUNc were similar to the bactericidal ones, with values ranging from 0.16 to 0.33 μg/mL, independently from their susceptibility pattern. The 90% of the investigated strains was inhibited in its growth at 0.33 μg/mL and a decrease of CFU counts, corresponding to ~7 $\log_{10,}$ was observed at MIC concentration in the treated samples after 24 hours of incubation. The citotoxicity test on AGS cells, evaluated by using MTT assay, demonstrated that SUNc is not toxic until concentrations between 1.30-2.62 μg/mL. The data obtained showed that SUNc is active against *Helicobacter pylori* and could represent a novel strategy for the treatment of the infection especially in cases of multidrug resistance.

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## P1.19 | The comparison of side effects of standard triple therapy and high-dose amoxicillin/bismuth therapy in eradication of *H. pylori*

**O. Sjomina**[1,2]; A. Lielause[1]; A. Rūdule[2]; E. Martinsone[2]; D. Pūpola[2,3]; R. Vangravs[2]; A. Kiršners[2]; S. Paršutins[2]; H. Gorskis[2]; I. Poļaka[2]; A. Jeniceka[1]; E. Cine[1]; G. Šķenders[2]; D. Razuka-Ebela[1]; M. Leja[1,2,4]

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**Background**: Antibiotics are standard treatment for *Helicobacter pylori*infection. A triple therapy including two antibiotics tends to cause wide spectrum of side effects, which may lead to therapy discontinuations and decrease of eradication rates. Objective: to compare side effects between two eradication regimens.

**Methods**: Clinical trial participants were healthy individuals aged 40-64. Eradication subgroup underwent urea breath test; positive patients were randomly divided into eradication subgroups - standard triple therapy (Amoxicillin 1 g x2, Clarithromycin 0.5 g x2 and Esomeprazol 0.04 g x2 - 14 days) and high-dose amoxicillin/bismuth therapy (Amoxicillin 1 g x3, Esomeprazol 0.04 g x2 and Bismuth subcitrate 0.24 g x2 - 14 days). Patients were contacted in 21-28 days; side effects and compliance were registered.

**Results**: By now, we acquired data from 157 patients with triple and 149 patients with bismuth therapy. Side effects were reported by 63.1% (n = 99) and 51.7% (n = 77) respectively. Mean number of side effects in triple therapy was higher ($P$ = 0.03): in standard triple therapy - 2.1 (median 2.0, deviation 1.25), while in bismuth therapy - mean 1.8 (1.0; 1.10).

**TABLE 1.** Side effects in different eradication regimens (**significant difference*)

| | Standard triple 14 days (n, %) | | High-dose amoxicillin/ bismuth, 14 days (n, %) | |
|---|---|---|---|---|
| Bitter taste* | 72 | 72.7% | 8 | 10.4% |
| Diarrhoea* | 36 | 36.4% | 16 | 20.8% |
| Nausea | 15 | 15.2% | 9 | 11.7% |
| Fatigue* | 14 | 14.1% | 5 | 6.5% |
| Bloating | 12 | 12.1% | 7 | 9.1% |
| Abdominal pain | 11 | 11.1% | 11 | 14.3% |
| Stool colour change* | 7 | 7.1% | 51 | 66.2% |
| Vomiting* | 6 | 6.1% | 0 | 0.0% |
| Skin rush | 5 | 5.1% | 5 | 6.5% |
| Sleep disorder | 5 | 5.1% | 6 | 7.8% |
| Flatulence | 4 | 4.0% | 3 | 3.9% |
| Skin itching | 3 | 3.0% | 4 | 5.2% |
| Epigastrial burning | 2 | 2.0% | 0 | 0.0% |
| Abdominal discomfort | 2 | 2.0% | 5 | 6.5% |

| | Standard triple 14 days (n, %) | | High-dose amoxicillin/ bismuth, 14 days (n, %) | |
|---|---|---|---|---|
| Loss of appetite | 2 | 2.0% | 0 | 0.0% |
| Vaginal discharge | 2 | 2.0% | 2 | 2.6% |
| Vertigo | 0 | 0.0% | 1 | 1.3% |
| Other | 3 | 3.0% | 5 | 6.5% |

Moreover, the compliance due to fewer side effects was higher: 96.3% vs 93.2% ($\chi^2$ = 4.1). Conclusions. Lower frequency of side effects provides better compliance and therefore increases chance of positive outcome. Reduction of antibiotic use may be beneficial to the microbiome in long term.

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## P1.20 | Pan-European registry on *Helicobacter pylori* management: results from Budapest, Hungary

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**Background**: The European Registry on *H. pylori* Management was set up by *Gisbert* and *McNicholl* et al in 2013 to monitor eradication practices in European countries for 10 years.

**Aim**: To assess the efficacy of different eradication regimens in a single outpatient clinic of gastroenterology.

**Methods**: Between 2013 and 2019, 247 patients were registered in a prospective non-interventional study. The infection was diagnosed either by endoscopy, histology, RUT or a $^{13}$C-UBT. As first-line treatment the patients received either a 7 days triple regimen (any of PPI + amoxicillin + clarithromycin or tinidazole), 10-day modified sequential treatment (PPI + amoxicillin for 5 days + followed by tinidazole and levofloxacin for 5 days), 10-day quadruple treatment (PPI + amoxicillin + tetracycline or doxycycline + metronidazole or tinidazole) or bismuth-based quadruple treatment (PPI + amoxicillin + tetracycline or doxycycline + metronidazole). Bismuth/non-bismuth-based quadruple or alternative regimens were given as second or third-line treatment. Controls were performed by an $^{13}$C-UBT.

**Results**: The eradication rates of different regimens are given in the Table.

**Conclusion**: Under real life settings in our district, the first-line concomitant regimen was significantly superior to triple therapies, but not significantly better than the sequential and bismuth-based treatment. Second- and third-line regimens achieved suboptimal results.

G.M. Buzás: None.

| Regimen | No. of cases | Duration (days) | ITT rates (%, 95% CI) | PP rates (%, 95% CI) | *P* vs triple therapy |
|---|---|---|---|---|---|
| Triple | 34 | 7 | 70.5 (54.4-86.7) | 82.7 (68.1-97.4 | - |
| Sequential | 60 | 10 | 76.7 (65.6-87.6) | 85.2 (75.4-94.9) | 0.05 |
| Concomitant | 70 | 10 | 84.3 (75.5-93.0) | 95.1 (89.6-100) | 0.03 |
| Bismuth quadruple | 36 | 10 | 80.5 (66.9-94.2 | 82.6 (69.7-95.9) | 0.08 |
| Second-line | 32 | 10-14 | 65.2 (48.2-83.0) | 70.0 (52.6-87.4) | - |
| Third-line | 11 | 10-14 | 54.5 (19.4-86.6) | 66.7 (28.-105.1) | - |

## P1.21 | Effect of *Helicobacter pylori* eradication on non-alcoholic fatty liver disease

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**Backgrounds**: Accumulating evidence has implicated *Helicobacter pylori* (*H. pylori*) infection in extra-gastric diseases such as cardiovascular diseases, neurological disorders, and metabolic diseases. Recently, many studies reported the association between *H. pylori* infection and nonalcoholic fatty liver disease (NAFLD), suggesting that *H. pylori* eradication might be an alternative method for the prevention or treatment of NAFLD. Thus, we examined the effect of *H. pylori* eradication on NAFLD improvement.

**Methods**: We performed a retrospective cohort study of 1,925 patients who were diagnosed *H. pylori* infection via gastric histology and then received *H. pylori* eradication. NAFLD status was diagnosed by ultrasonography and classified into 4 groups based on baseline and follow-up findings: no change, improved, or aggravated. We also calculated the NAFLD fibrosis score as an index of liver fibrosis.

**Results**: After treatment for *H. pylori* eradication, 1,474 patients succeeded in eradication and the remaining 451 patients failed. In the group with successful eradication, the proportion of patients who had NAFLD improvement, assessed by ultrasound, was 10.8%. In the group with unsuccessful eradication, the proportion of patients who had NAFLD improvement was 13.4%. There was no significant difference in NAFLD improvement between the two groups ($P = 0.074$). In the analysis by NAFLD fibrosis score, no significant difference in NAFLD improvement was showed between the two groups ($P = 0.399$).

**Conclusions**: Our findings showed that *H. pylori* eradication had no effect on NAFLD improvement, assessed by ultrasound and NAFLD fibrosis score.

H. Lee: None. T. Kim: None. Y. Park: None. J. Lee: None. J. Kim: None.

## P1.22 | Testing and treatment of *Helicobacter pylori* infection among patients with Lynch syndrome: The MD anderson cancer center experience

**S. Thirumurthi**[1]; P. Lum[1]; D. Y. Graham[2]

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Lynch syndrome (hereditary non-polyposis colon cancer) is an inherited condition with mutations in one of the DNA mismatch repair genes. Patients have an 80% lifetime risk of colon cancer and are at an increased risk for gastric cancer. Routine upper endoscopy (EGD) for surveillance should be performed with testing and treatment for *H. pylori* infection. The aim of our quality improvement study was to determine adherence to EGD surveillance, rate of biopsy and treatment of *H. pylori* infection in this patient population.

**Methods**: All patients with Lynch syndrome who underwent EGD 2001-2018 and histopathology reports were identified using natural language processing. Charts were reviewed for treatment information.

**Results**: A total of 598 patients underwent endoscopy during the study period. There were 1293 EGDs done in 496 patients during the study period (102 patients had no EGD, surveillance rate 82.9%). Gastric biopsies taken during 842 exams (281 patients) identified 26 unique patients with *H. pylori* infection (65.1% biopsy rate, 34.9% no biopsy taken). Treatment was documented in 19/26 patients (overall treatment rate 73%, compliance with eradication testing rate 79%, successful eradication rate 64.4%) (Table1).

**Discussion**: *H. pylori* infection is a reversible risk factor for both sporadic and hereditary gastric cancer and important in risk reduction. A quality improvement protocol will be implemented to assess, treat and confirm cure of *H. pylori* infection in Lynch syndrome patients.

**Patients positive for *H. pylori* infection n = 26**

| | Lynch syndrome confirmed | Lynch syndrome suspected |
|---|---|---|
| Genetic mutation | N = 19 | N = 8 |
| MLH1 | 6 | x |
| MSH2 | 9 | x |
| MSH6 | 3 | x |
| PMS2 | 1 | x |
| Gender | | |
| Male | 12 | 5 |
| Female | 7 | 3 |
| Race | | |
| White | 13 | 1 |
| Hispanic | 2 | 2 |
| Asian | 2 | 1 |
| Black | 1 | 1 |
| Not reported | 1 | 2 |
| *H. Pylori* treatment regimen | | |
| Quadruple therapy | 6 | 1 |
| Triple therapy | 7 | 5 |
| Total gastrectomy | 1 | 0 |
| No therapy | 5 | 2 |
| Treatment rate | 72.2% | 75.0% |
| Eradication testing in medically treated Patients | | |
| Completed, eradication confirmed | 7 | 4 |
| Test pending | 4 | 0 |
| Test not ordered | 4 | 2 |
| No documented therapy but eradication documented | 2 | 0 |
| Eradication rate | 53.8% | 75.0% |

S. Thirumurthi: None. P. Lum: None. D.Y. Graham: None.

## P1.24 | Alterations in cholesterols of *H. pylori* cell membrane upon exposure to PPIs

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**Introduction**: Cholesterol in *H. pylori* cell membrane becomes glucosylated, yielding cholesteryl-α-D-glucopyranoside (CG). Attachment of acyl group to CG leads to cholesteryl-60-O-acyl-a-Dglucopyranoside (CAG). Attachment of phosphatidyl group to CG leads to cholesteryl-60-O-phosphatidyl-a-Dglucopyranoside (CPG). Cholesteryl glucosides (CGs) are essential for *H. pylori* cell division and stress response. This study examined proton pump inhibitors (PPIs) effect on CGs of *H. pylori* cell membrane.

**Method**: PPIs were added to flasks containing BHI broth and 2.5% serum, to reach concentrations of omeprazole (OMP) 32 μg/mL, lansoprazole (LZP) 8 μg/mL and pantoprazole (PAN) 128 μg/mL. A fresh culture of one *H. pylori* isolate was inoculated into flasks with final turbidities of McFarland No.2. Untreated culture was a control. Cultures were incubated under microaerophilic conditions at 37°C. After 24 hours bacterial cells were washed and resuspended in PBS. A 50 μL volume of bacteria was cultured on Brucella blood agar for growth. Harvested bacteria were used for cholesterol extraction. Bacterial GCs contents were analyzed by Gas chromatography.

**Results**: Treated cells cultures were negative. Analysis of CGs of control *H. pylori* showed occurrence of all cholesterols, CG (79.58%), CAG (17.40%) and CPG (3.02%). In treated cells, CAG was detected as total cholesterol components (100%), however CG and CPG were not detected.

**Conclusion**: Acylated cholesterols like CAG are important for bacterial cell integrity under stressful conditions. Accumulation of CAG in PPIs-treated *H. pylori* might indicate bacterial strategy for survival. Since phospholipids have been regarded essential for bacterial cell division, growth inhibition in treated *H. pylori* could be due to lack of CPG content.

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## P1.25 | Use of probiotics in the *Helicobacter pylori* eradication in Italy: data from the Italian Registry on *Helicobacter pylori* treatment

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**Background**: Probiotics may have beneficial effect in reducing adverse events in patients treated for *Helicobacter (H.) pylori* infection; however, data on their use in this setting are scarce.

**Aim**: To investigate the use of probiotic supplementation in the treatment of *H. pylori* infection in clinical practice in Italy.

**Methods**: The "Italian Registry on *H. pylori* treatment" is an online database prospectively registering adult patients prescribed with a treatment for *H. pylori* infection by gastroenterologists in Italy. Data were collected in 17 Centers from June 2017 to May 2019 using the web application REDCap (Research Electronic Data Capture).

**Results**: A total of 1803 patients [1140 (63.5%) females, mean age (SD): 55.4 years (15.1)] were included in the Registry in the study period. Of these, 1699 received one treatment regimen, 101 two regimens and 3 three regimens, with a total of 1910 cases. Probiotics were prescribed in 49.9% (n. 953) of cases: 100% (61/61) with rifabutin triple therapy, 86.4% (472/546) with sequential therapy, 54.2% (77/142) with levofloxacin triple therapy, 46.3% (38/82) with concomitant therapy, 33% (211/641) with bismuth quadruple therapy (Pylera®), 24.1% (90/374) with clarithromycin triple therapy and 21.1% (4/19) with other regimens. The most frequently prescribed probiotic was a combination of *Lactobacillus rhamnosus* and *Bifidobacterium breve* (586, 61.5%), followed by *Lactobacillus casei DG* (118, 12.4%), *Lactobacillus rhamnosus* (85, 8.9%), *Saccaromyces boulardii* (74, 7.8%) and others probiotics (90, 9.4%). Conclusions

Probiotic supplementation is used in half of patients treated for *H. pylori* eradication in Italy. *Lactobacillus* and *Bifidobacterium* are the probiotics most commonly prescribed.

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## P1.26 | The Effect of Rabeprazole Dosing Timing on *Helicobacter pylori* Eradication Efficacy

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**Background/Aims**: Thirty minutes pre-prandial dosing has been considered a prerequisite for proper PPI effect. Pre-prandial intake is quite bothersome. Rabeprazole has recently been proved to use postprandially as well as pre-prandial dosing. We investigated the Helicobacter eradication efficacy of postprandial rabeprazole dosing compared to pre-prandial PPI regimen.

**Materials and Methods**: Study was conducted by review of electronic medical record of patients who received triplet regimen (rabeprazole, amoxicillin, and clarithromycin) at an academic institute, Seoul, from January 2016 to January 2019.

**Results**: A total of 340 subjects were enrolled consecutively. Eight-six subjects were excluded due to incomplete data profiles. Finally, 254 subjects were included in the analysis. One hundred and thirty-five subjects (control group) were treated with pre-prandial rabeprazole and 119 subjects (test group) were with postprandial dose. The mean ages were 52.6 (±12.5) year old for the control group and 56.1 (±11.9) for the test group. The male to female ratios were 1.65 (84/51) for the control group and 1.90 (78/41) for the test group. *Helicobacter pylori* eradication was successful in 79.2% in total. In control group 79.3% was successful and in test group 79.2% was successful (*P*-value = 0.474). In subgroup analysis, the 14-day regimen showed better eradication success rate than 7-day regimen, 85.5%, and 72.8% respectively, but statistical significance was not achieved (*P*-value = 0.55). Gender, smoking, alcohol, and comorbidities have no impact on eradication efficacy.

**Conclusion**: For *Helicobacter pylori* eradication, postprandial rabeprazole dosing results in a comparable success rate to pre-prandial dosing in a rabeprazole-amoxicillin-clarithromycin combination regimen.

D. Cheung: None. S. Suk: None. S. Kim: None. S. Park: None.

## P1.27 | Comparison of the eradication rate of second-line treatment according to the type of first-line therapies in *Helicobacter pylori*

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**Background/Aims**: Various therapies have been tried to overcome the antibiotics resistance of *Helicobacter pylori*. However, little is known about the results of second-line treatment of these first-line therapies. We compared the eradication rates of second-line treatment according to first-line therapy.

**Method**: We analyzed 275 patients who showed positive findings on urea breath test (UBT) after first-line treatment of *H. pylori* infection from January 2014 to December 2018 in our hospital. First-line treatment regimen was defined as follows; (1) triple therapy (2) concomitant therapy (3) sequential therapy (4) hybrid therapy. All the patients took bismuth containing quadruple therapy (PBMT) for second-line treatment.

**Result**: Among 275 patients, 166 patients underwent second-line treatment of *H. pylori* and result of UBT after second-line treatment was confirmed in 132 patients. The eradication rate of second-line treatment were 82.6% (109/132) in all patients. The eradication rate according to the type of first-line treatment was as follows. 83.3% (60/72) for triple therapy, 84.6% (33/39) for concomitant therapy, 73.3% (11/15) for sequential therapy, 83.3% (5/6) for hybrid therapy ($P$ = 0.757). There was no significant difference in eradication rate among the most frequent three regimen (triple therapy, concomitant therapy and sequential therapy, $P$ = 0.595).

**Conclusion**: There was no significant difference in eradication rate of second-line PBMT therapy according to first-line therapy. Therefore, bismuth containing quadruple therapy is acceptable for the second-line treatment for eradication of *H. pylori*.

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## P1.28 | Sertraline - an anti-depressive compound with an activity against *Helicobacter pylori*

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**Introduction**: One of the greatest challenges of modern therapeutic therapies directed towards *Helicobacter pylori* is the increasing resistance of this bacterium to antibiotics. This phenomenon has contributed in recent years to a significant increase in scientific reports indicating the possibility of using new, alternative substances in the fight against this pathogen.

**Aim**: To determine the activity of sertraline, a substance with antidepressive activity, against clinical and reference *H. pylori* strains.

**Methods**: The study of antimicrobial activity of sertraline against *H. pylori* strains was performed by the disk-diffusion and microtitration methods. The study was extended to analyze the interaction of sertraline with selected antibiotics (amoxicillin, clarithromycin, metronidazole and tetracycline) using the checkerboard method. In addition, the effect of sertraline on the *H. pylori* morphology was determined by light and scanning electron microscopy.

**Results**: Growth inhibition zones produced by sertraline were in the ranges of 10-25 mm, 17-33 mm and 19-37 mm for discs containing 0.2 g, 1 g and 2 g, respectively. The minimum inhibitory concentrations (MICs) and minimum bactericidal concentrations (MBCs) counted for 2-8 μg/mL and 4-8 μg/mL, respectively. It was observed that the MICs did not stimulate the transformation of *H. pylori* into coccoid forms, whereas at MBC values they were the dominant morphotype. In the checkerboard assay, a synergistic/additive interaction of sertraline with all four antibiotics tested was observed.

**Conclusion**: Obtained results indicate a high *in vitro* antimicrobial activity of sertraline against *H. pylori*.

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## P1.29 | Management of *Helicobacter pylori*infection by clinicians in a developing country: a questionnaire analysis with latitudinal and longitudinal comparison

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**Background & Aims**: Practices deviating from the consensus means the inefficient management of *Helicobacter pylori*(*H. pylori*). The study aims to investigate attitude changes and influence factors in the management of *H. pylori* infection among the Chinese clinicians.

**Methods**: An authoritative online questionnaire was distributed to nationwide clinicians who participated in 14th (2014) or 17th (2017) Congress of Gastroenterology China. The *Fifth Chinese National Consensus Report on the management of H. pylori infection* was invoked as the criterion to evaluate the deviation from consensus.

**Results**: A total of 4182 valid samples were included in the study. More than 60% of the respondents were gastroenterologists worked in tertiary hospitals. Respondents had a different level of cognition to *H. pylori*-related diseases, ranging from 45% to 95% of the total. Up to 40% of the respondents did not follow the recommendations for the diagnosis of *H. pylori*. The choices of eradication regimens and antibiotic combinations were not ideal. About 20% of the respondents did not pay attention to the confirmation after the eradication. The embarrassing situation has alleviated reassuringly in 2017 compared with that in 2014. Multivariate logical regression analysis showed that specialty (non-gastroenterologist), degree (undergraduate and below), and age (<35) were the main influence factors for the difference in practices (all $P < 0.001$).

**Conclusions**: Current management towards *H. pylori* infection have been improved inspiringly, while there is still a gap between the real-world practices and the consensus. Partial individual factors should be taken into account for decision-making to implement the guideline.

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## P1.30 | Second line bismuth-containing quadruple therapy for *Helicobacter pylori* eradication in Korea

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**Background**: Bismuth-containing quadruple therapy (BQT) is recommended for the second-line eradication treatment if the clarithromycin-based triple therapy fails by the Maastricht IV/Florence consensus report.

**Aim**: To evaluate *Helicobacter pylori (H. pylori)* eradication rates of BQT as second-line therapy in South Korea.

**Methods**: From 2009 to 2018, the medical records of 562 patients who underwent second-line BQT were retrospectively reviewed in St. Paul's Hospital, Catholic Medical Center, Korea.

BQT (PPI + bismuth + metronidazole+ tetracycline) was prescribed for 7, 10 or 14 days. This study compared 7- with 10-14 days by the

treatment duration. *H. pylori eradication* was confirmed by a $^{13}$C-urea breath test at least 4 weeks after completion of treatment. The eradication rates was determined by intention-to-treat (ITT) and per-protocol (PP) analyses.

**Results**: The ITT eradication rates were 79.1% (400/506; 95% CI: 75.6%-82.6%) and 76.8% (43/56; 95% CI: 65.7-87.9%) with the 7- and 10-14 day regimen, respectively ($P$ = 0.838). The eradication rates by PP analyses were 92.6% (398/430; 95% CI: 90.1%-95.1%) in the BQT 7 group and 91.5% (43/47; 95% CI: 83.5%-99.5%) in the BQT 10-14 group ($P$ > 0.999). The eradication rates by PP analysis over the past decade are not different.

**Conclusion**: The use of bismuth-containing quadruple therapy as second-line therapy is effective in Korea.

M. Cho: None. H. Hwang: None. Y. Kim: None. C. Lim: None. J. Oh: None.

## P1.31 | Effects of the combination of *Saccharomyces boulardii* with sequential therapy in the eradication of *Helicobacter pylori*: A prospective randomized controlled study

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Eradication of *Helicobacter pylori*, remains valid because of constantly evolving data. Recent Maastricht V recommendations stipulate that concomitant quadritherapy and bismuth therapy take place on sequential treatment because of a higher eradication rate. Goal: study the effects of the combination of probiotics with sequential therapy on HP eradication rates and the incidence of adverse events.

**Patients and Methods**: 99 patients with documented HP infection, May 2014 May 2017, two groups: control group receiving a standard sequential therapy comprising a daily double dose of Omeprazole, Amoxicillin for the first 5 days, followed double dose of Omeprazole 20 mg, Clarithromycin 500 mg, Metronidazole 500 mg for 5 days later, and an experimental group receiving the same protocol associated with a double daily intake of 250 mg of Saccharomyces Boulardii.

**Results**: Two groups were matched in terms mean age = 44.3 vs 43 years, ratio H/F 1.15, medical history, smoking, endoscopic, histological. In intent to treat ITT and per PP protocol, the eradication rate was significantly higher for the experimental group (86.6% ITT, 87.5% PP) compared to the control group (78.2% ITT 74.7%).$P$ = 0.02. The combination of SB significantly decreased the rate of adverse reactions overall (RR = 0.26)the rate of onset of diarrhea (RR = 0.07) and also reduced the rate of onset of nausea, asthenia and metallic taste, but this not statistically significant. In multi-variate analysis, SB is associated with optimization of the eradication rate (RR = 2.4, $P$ = 0.02), and a decrease in the rate of eradication.

**Conclusion**: Based on our results, combination of SB with sequential treatment allows a significant reduction of the adverse effects, especially of antibiotic-related diarrhea, an optimization of the rate of HP.

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## P1.32 | Inhibition of *Helicobacter pylori* growth by different probiotics and autoprobiotics in vitro

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Probiotics used for the eradication of *Helicobacter pylori* infection (HPI) are not always effective. They can have low anti-helicobacter activity and quickly eliminate from the organism. Autoprobiotics, non-pathogenic bacteria isolated from the organism and introduced into it for therapeutic purposes have advantages comparing with probiotics: immunological tolerance and the absence of confrontations with the microbiome (Suvorov, 2017). Aim: to compare the anti-helicobacter action of different probiotic and autoprobiotic enterococci in vitro. The anti-helicobacter activity of probiotic strains *Enterococcus faecium*L3 (L3), *E. faecium*SF-68 (SF) and 10 autoprobiotic *E.faecium* (AP), isolated from stomach and gut of patients with HPI was studied. Genome of AP was monitored for the presence of 10 putative virulence genes and genes coding enterocins production by PCR. The activity of enterococci was evaluated by spot-on-lawn assays (8 lgCFU/mL).Zones of growth inhibition (ZI, 3-15 mm) were detected after incubation of H.p. in anaerobic condition during 5 days. H.p. strains have shown different sensitivity to probiotics and AP. L3, SF and AP inhibited the growth of HP for 79%, 64% and 60-78% relatively. AP differ in the activity against H.p. Two strains AP were more active than probiotics (ZI = 13-15 mm). The results demonstrate: 1. Relative high anti-helicobacter activity of AP, L3, SF; 2. The need to select probiotics and AP for the treatment of H.p. infection.3. high perspectives for the search for new probiotic strains with more activity against H.p. The study was supported by Russian Science Foundation 16-15-10085.

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## P1.33 | The efficacy of Lactobacillus acidophilus and rhamnosus in the modification of gut microbiota and reduction of *Helicobacter pylori* bacterial load- a double-blind, placebo-controlled, randomized trial

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**Background/Aims**: We aimed to assess the efficacy of Lactobacillus acidophilus and Lactobacillus rhamnosus in the reduction of bacterial load of *H. pylori* and modification of gut microbiota.

**Methods**: In this double-blind, randomized, placebo-controlled trial, we recruited adult subjects with *H. pylori* infection. Eligible subjects were randomized to receive (1) probiotic containing Lactobacillus acidophilus and Lactobacillus rhamnosus or (2) placebo, all given twice daily for 4 weeks. $^{13}$C-UBT was determined and fecal specimens were collected before treatment and weekly during treatment until 2 weeks after the end of treatment. Amplification of the V3 and V4 hypervariable regions of the 16S rRNA was done followed by high throughput sequencing.

**Results**: A total of 40 subjects were randomized to receive probiotic (N = 20) or placebo(N = 20). DOB value was significantly lower in the probiotic group than in placebo group at the end(4 weeks) of treatment (DOB 26.0 vs 18.5, $P$ = 0.045). DOB value was significantly reduced compared to baseline in the probiotic group (18.5 vs 26.7, $P$ = 0.001), but not in the placebo group(26.0 vs 25.0, $P$ = 0.648). There were no significant changes in the α-diversity at week 4 compared to baseline in the probiotic group ($P$ = 0.91) and the placebo group ($P$ = 0.89). There were neither significant changes in the β-diversity at week 4 compared to baseline in the probiotic group ($P$ = 0.997) and the placebo group ($P$ = 0.983).

**Conclusions**: The use of Lactobacillus acidophilus and rhamnosus may reduce the bacterial load of *H. pylori*. There were no significant changes in the composition of gut microbiota after the probiotics.

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## P1.34 | The effect of PPI pre-administration on *Helicobacter pylori* eradication efficacy

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**Background/Aims**: Intragastric acid suppression is a key factor in successful *Helicobacter pylori* eradication. Proton pump inhibitors (PPIs) require about 5 days to fully saturate acid pumps on parietal cells and to achieve the maximal and steady effect. We investigated the effect of 5 or more days rabeprazole pre-administration on *Helicobacter pylori* eradication efficacy.

**Materials and Methods**: Study was conducted by retrospective review of the electronic medical record of patients who received triplet regimen (rabeprazole, amoxicillin, and clarithromycin) at an academic institute, Seoul, from January 2016 to January 2019.

**Results**: A total of 340 subjects were enrolled consecutively. Sixty-six subjects were received PPI ≥ 5 days before eradication regimen for various reasons including patients' wishes, pre-existing acid-related symptom control, the possibility of other drug interaction, and so on (test group). One hundred and seventy subjects who took eradication regimen without pre-administration of PPI were enrolled during the study period (control group). In control group, the eradication success rate was 69.9% (58/83) for 7-day regimen and 87.4% (76/87) for 14-day regimen, respectively ($P$-value = 0.004). In test group, the eradication success rate was 75.8% (25/33) for 7-day regimen and 81.8% (27/33) for 14-day regimen, respectively ($P$-value = 0.382). In those who received 7-day regimen, there was a tendency of higher eradication rate in PPI pre-administered subjects, however, power did not reach the statistical significance. Gender, smoking, alcohol, and comorbidities have no impact on eradication efficacy.

**Conclusion**: For *Helicobacter pylori* eradication, PPI pre-administration ≥ 5 days abolishes the difference between 7-day and 14-day regimen.

Y. Park: None. D. Cheung: None. J. Kim: None. S. Park: None.

## P1.35 | Randomized controlled study to see the effects of a triple therapy including vonoprazan or rabeprazole for the second-line treatment

**M. Hojo**; K. Matsumoto; K. Izumi; N. Yatagai; Y. Akazawa; T. Takeda; K. Ueda; H. Ueyama; Y. Shimada; H. Sasaki; K. Matsumoto; D. Asaoka; A. Nagahara

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**Background**: Inhibition of gastric acid is important for eradicating *Helicobacter pylori*. Vonoprazan (VPZ) is a strong and long-lasting acid-inhibitor. Phase III randomized trial indicated that VPZ was effective in the first-line triple therapy. Recently, studies to examine the effect of triple therapy including VPZ in the second-line treatment have been made. But, few prospective studies on the effect of triple therapy including VPZ were performed, and it is not known which more effective between second-line triple therapy including VPZ or PPI. [Aim] This study aimed to examine the difference in efficacy and safety between second-line triple therapies including VPZ and rabeprazole (RPZ) as a PPI.

**Methods**: Eligible patients who failed the first-line triple therapy and received written informed consent were randomly assigned to VPZ group [40 mg/day VPZ, 1500 mg/day amoxicillin (AMPC), 500 mg/day metronidazole (MNZ)] and RPZ group (20 mg/day RPZ, 1500 mg/day AMPC, 500 mg/day MNZ). Assessment was done for over 4 weeks after the treatment. Less than 2.5‰ in the 13C-urea breath test was considered as successful eradication.

Analysis of efficacy and side effects were performed based on the full analysis set.

**Results**: Patients were assigned to VPZ group (n = 21: M/F = 10/11, mean 57 ± 11 years old) and RPZ group (n = 23: M/F = 14/9, mean 57 ± 14 years old). Successful eradication rates in the VPZ and RPZ groups were 81% and 82.6%, respectively ($P$ = 1.00). Two patients of VPZ and a patient of RPZ group discontinued due to side-effects ($P$ = 0.60).

**Conclusion**: There was no significant difference in efficacy and safety between the second-line therapies including VPZ and RPZ.

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## P1.36 | Inhibitory effects of ß-caryophyllene on *Helicobacter pylori* infection: a randomized double-blind, placebo-controlled study

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**Background**: *Helicobacter pylori* infection is a common disease in South Korea, that causes various gastroenteral symptoms, and its eradication rate is decreased lately. β-Caryophyllene is a natural bicyclic sesquiterpene that found in a wide range of plant species from cloves, basil, and cinnamon. ß-caryophyllene is reported to have anti-inflammatory and anti-bacterial effects. We tried to evaluate the inhibitory effect of ß-caryophyllene to *H. pylori* infection, and its possibility of use as an alternative gastroenteral drug.

**Method**: The study was a 8-week, randomized double-blind, placebo-controlled trial of subjects to two groups (ß-caryophyllene 126 mg and placebo per day). Thirty-three were treated with ß-caryophyllene and 33 were given a placebo. Inflammation level of *H. pylori* infiltration and eradication rates were measured through endoscopy and UBT in both groups before and after the dose. And serum cytokine (tumor necrosis factor-α (TNF-α), interleukin-1ß (IL-1ß), interleukin-6 (IL-6)) was compared in both groups before and after the medication.

**Results**: Complete eradication was not found in both groups. Also no significant change in UBT, updated Sydney score was found. However, only ß-caryophyllene group showed statistically significant improvement in nausea ($P$ = 0.025), epigastric pain ($P$ = 0.018), also decrease in serum IL-1ß level ($P$ = 0.038).

**Conclusion**: Single administration of ß-caryophyllene can be considered as an alternative therapy for eradication of *H. pylori* and relieving symptom of dyspepsia.

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## P1.37 | Patient education materials to improve care of *Helicobacter pylori* infection: development of new tools in collaboration with patients and health professionals

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**Background**: In 2017, the French National Authority for Health and the National Council of gastroenterologists published guidelines for professionals on *Helicobacter pylori* infection to promote appropriate practices. Patient information and involvement in decision making has been proven to improve compliance and reduce treatment failure. Consequently, two information sheets on diagnosis and treatment of *Helicobacter pylori* infection were developed.

**Methods**: Both sheets were elaborated together with patients and healthcare professionals. The development process included: i) production of a first draft by a multidisciplinary working group (4 patients, 1 general practitioner, 2 gastroenterologists and1 pharmacist), ii) test phase conducted with two focus groups (17 patients recruited via social networks) in order to ensure a good understanding of the messages, the presence of all the information deemed important and to assess the attractiveness of the sheets, iii) correction and finalization.

**Results**: Two double-sided sheets, easily printable, were developed. The first-one describes indications and methods for *Helicobacter pylori* diagnosis. The second-one explains the principles of treatment, specifies its efficacy and expected adverse effects, and emphasizes the importance of adherence and control. Patients from the focus-group found the documents educational, incentive and reassuring on a subject that they considered complex. The sheets are complemented by a Frequently Asked Questions only available on the website in French and in English (www.has-sante.fr).

**Conclusion**: These patient information sheets are intended to support and complement oral information given by the physician. They should help patients and physicians to elaborate together an appropriate diagnosis and treatment plan.

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## P1.38 | Management of *Helicobacter pylori* infection in Russian clinical practice

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**Background**: *Helicobacter pylori* (*H. pylori*) infection treatment is still a challenge for clinicians. Eradication rates have fallen in the last 20 years and remain a problem of the real world practice.

**Objectives and Methods**: In the framework of the project "Real clinical practice of treating acid-related diseases" we evaluated management of 1474 *H. pylori* (+) patients who applied to 188 doctors in Moscow and Saint-Petersburg. Patients were managed with the original Registry of *H. pylori* infection.

**Results**: 1474 *H. pylori* (+) patients were included in Registry and 1330 patients were analyzed after eradication therapy (ET). Average age was 45.7 years, 66% were female. 10% of patients took antibiotics during past 6 months (17% macrolides). *H. pylori*-associated diseases were: chronic gastritis (48.6%), peptic ulcer disease (20.6%). $^{13}$C-urea breath test was used in 20% and rapid urease tests in 73.2% for diagnosis of *H. pylori*. First-line regimens included triple ET reinforced with bismuth (71.2%), classic triple therapy (18.8%), hybrid therapy without bismuth (7.4%), others (2.9%). Rabeprazole was prescribed in 95.8%. The probiotic Pylopass was added in 57.1% cases. ET was successful in 92.0% (ITT-analysis) and in 95.5% (PP-analysis) cases. Adverse events occurred in 19.9%.

**Conclusion**: Management of *H. pylori* infection by Russian physicians is heterogeneous. First choice in most cases was noncanonic qaudro-bismuth-base therapy with PPI, clarithromycin and amoxicillin. Treatment with rabeprazole is able to achieve over 95% eradication rates. More than 50% physicians recommended probiotic Pylopass with antibiotics. In spite of using macrolides in anamnesis, ET was effective in 92% (ITT).

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## P1.39 | The effect of rebamipide therapy on eradication rates and side effects during triple therapy of *Helicobacter pylori* infection

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**Backgrounds/Aim**: Previous studies reported that rebamipide improve the effectiveness of *Helicobacter pylori* (*H. pylori*) eradication therapy. However, effect of rebamipide on possible reduction of side effects remained controversial. This study was performed to evaluate whether the addition of rebamipide to proton pump inhibitor (PPI)-based triple therapy decreases the eradication rates and side effects.

**Methods**: We reviewed 61 patients who were infected with *H. pylori* and treated with triple therapy plus rebamipide. The triple therapy consisted of lansoprazole 30 mg b.i.d., clarithromycin 500 mg b.i.d., and amoxicillin 1 g b.i.d. for 7 days. The patients received rebamipide or not for 7 days starting from the first day of triple therapy. Eradication rates were obtained by urea breath test performed 4 weeks after completion of triple therapy. Adverse events and complications were evaluated by symptom questionnaires after 7, 14, 21 and 28 days of the treatment.

**Results**: 35 patients were treated with triple therapy plus rebamipide (Group A) and another 26 patients without rebamipide (Group B). *H. pylori* eradication rates was 60% (21 of 35) in group A and 53.8% (14 of 26) in group B. Two major side effects are reflux symptom and epigastric discomfort. There was no noticeable difference in side effect between two groups. Most adverse events were mild to moderate in intensity.

**Conclusion**: The addition of rebamipide to triple therapy might be effective on the boosting eradication rates than without rebamipide. The side effects were mostly reduced after 4 weeks of eradication treatment.

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## P1.40 | Amoxicillin transfer across the gastric mucosa in the rat model of atrophic gastritis

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**Background**: The transfer rate of antibiotics from the bloodstream to the stomach lumen largely affects the efficacy of *H. pylori* eradication.

**Methods**: To evaluate gastric secretion of antibiotics in atrophic gastritis (AG) we used a model similar to described by Noguchi et al. in 2007. Fifteen 4-6-week old male rats from the experimental group drank 0.2% ammonia aquatic solution for 12 weeks. Additionally, they received 60% ethanol (1 mL/100 g of body weight) by gavage twice a week. Age matching control group (n = 14) was not treated with chemicals. During the experiment, animals from both groups were injected with amoxicillin (50 mg/kg, i.v.) and washes from the gastric mucosa were sampled 30-240 minutes later. Concentration of amoxicillin in samples was assessed using chromatography-mass spectrometry.

**Results**: Rats from the experimental group demonstrated morphological and immunohistochemical features of fundic and antral AG in contrast to controls. Additionally, macroscopic examination revealed hyperemia and erosions of the mucosa witnessing exacerbation of gastritis. Amoxicillin level was significantly higher in the experimental group ($P < 0.01$, Mann-Whitney U test). Mean concentrations (ng/mL) in the control vs experimental group were: at 30th min - 425 and 1100; at 60th min - 312 and 1148; at 120th min - 341 and 1234; at 240th min - 215 and 928.

**Conclusion**: Erosions against a background of AG enhance the transfer of amoxicillin into the gastric lumen that might be relevant for *H. pylori* eradication.

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## P1.41 | Gastric microbiota and probiotics opportunities in *Helicobacter pylori* eradication in children

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Probiotics can have a direct antagonistic effect on *H. pylori*. The study was conducted from 2015–2017 St. Petersburg Children's City Clinical Hospital No. 5. In 103 patients aged 9 to 17 years (55 boys and 49 girls) with histologically confirmed *H. pylori*-associated chronic gastritis a double-blind, randomized, placebo-controlled study of the effectiveness of L. reuteri DSMZ17648 was performed both as monotherapy and an adjuvant to eradication therapy (omeprazole + amoxicillin + metronidazole + bismuth-OAMB for 10 days). The L. reuteri course in subgroup A lasted for 28 days and in subgroup B for 56 days. The control was performed by endoscopy, histology, rapid urease test (RUT), ammonia breath test (ABT), *H. pylori* count in the biopsy, inflammatory, and atrophic indices. In eight *H. pylori* (+) and eight *H. pylori* (-) children, sequencing of 16S-rRNA microbiota in biopsies of gastric mucosa was carried out. *H. pylori* decreased microbial diversity associated with inflammation and focal mucosal atrophy. *H. pylori* eradication was achieved on L. reuteri monotherapy in 50% after 28 and 60% after 56 days; on adjuvant L. reuteri 60% after 28 and 77.8% after 56 days; and in the placebo group 68.8% after 28 and 56 days. Clinical manifestation, inflammatory, and atrophic changes during L. reuteri treatment significantly and reliably decreased. We believe that in children L. reuteri DSMZ17648 monotherapy has advantages over standard triple therapy as it better cures clinical manifestation and gastric mucosa inflammation due to the correction of the state of gastric microbiota as a whole.

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## P1.42 | Anti- bacterial activity of H2-blockers and vitamins B1 and B6 against *H. pylori*

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**Background**: Antibiotic resistance of *H. pylori* is a major problem in treatment of dyspeptic patients. In this study the anti-*H. pylori* effect of H2-blockers ranitidine (RAN), famotidine (FAM) and cimetidine (CIM) as well as vitamins B1(Vit B1) and B6 (Vit B6) was examined by agar dilution method.

**Methods**: Five *H. pylori* isolates from gastric biopsies of patients with dyspepsia were treated with FAM and RAN (1,000 and 2,000 μg/mL), CIM (100 μg/mL) and Vit B1 and B6 (5,000 and 10,000 μg/mL). Drugs were added to Brucella blood agar and the suspension from each bacterial isolate with the turbidity of McFarland No 2 was spot inoculated on the plates. Results were recorded after 7 days of microaerobic incubation at 37°C.

**Results**: Examination of plates showed that *H. pylori* growth was inhibited by 100 μg/mL of CIM and 2000 μg/mL of FAM and RAN. Furthermore, Vit B1 and B6 both inhibited the growth of all 5 *H. pylori* isolates at 10000 μg/mL.

**Conclusions**: Antibacterial activity of vitamins on several bacteria such as *Staphylococcus aureus* and *Escherichia coli* has been reported. Results of this study showed that vitamins B1 and B6 could also inhibit *H. pylori* growth. Moreover, the recruited H2-blockers exerted antibacterial effect on *H. pylori*. In contrast to H2-blockers, vitamins B1 and B6 were effective at concentrations much higher than H2-blockers. Using vitamins and H2-blockers as substitutes or complements in eradication therapies against *H. pylori* can be suggested, although the mechanism of action of these drugs remains to be elucidated.

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## P1.43 | Nonpharmacologic remedies improve eradication of *Helicobacter pylori* in patients with duodenal ulcer

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**Purpose**: To elaborate the optimal *Helicobacter pylori* eradication regimens in duodenal ulcer patients using nonpharmacologic remedies.

**Methods**: In this study250 *Helicobacter pylori*-positive duodenal ulcer patients were randomized into 5 groups, 50 patients in each. Histological detection of *Helicobacter pylori*, intragastric and intraduodenal pH-metry were performed. Eradication regimens included: Group I -amoxicillin, clarithromycin, PPIs 10-days, PPIs then 20-days; Group II - the same treatment plus probiotics, containing Lactobacillus bulgaricus, Lactobacillus rhamnosus, Lactobacillus acidophilus and Bifidobacterium during one month; Group III - PPIs, probiotics and alkaline hydrocarbonate-chloride sodium mineral water, one month; Group IV - PPIs, probiotics and chloride sodium mineral water, one month;; Group V - probiotics and PPIs twice daily, one month.

**Results**: 82% of patients had dyspeptic complaints. In 50% of patients of Group I increased frequency of dyspeptic complaints. Disappearance of dyspeptic complaints was 74%, 78%, 76% and 74% in II, III, IV and V groups respectively. The eradication rate were 70%, 82%, 80%, 78% and 68% in I, II, III, IV and V groups, respectively. Healing of duodenal ulcer were in 82%, 84%, 86%, 84% and 78% of cases, in I, II, III, IV and V groups, respectively. Intragastric and intraduodenal pH increased in all groups, especially in III.

**Conclusions**: Triple eradication therapy increases the frequency of dyspeptic complaints, has low efficacy (70%). Adding probiotics improves efficacy of *Helicobacter pylori* eradication (82%). The combined use of PPIs, probiotics and mineral water is a highly effective and low-cost alternative therapy in patients with *Helicobacter pylori*-associated duodenal ulcer.

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## P1.44 | Inhibitory effects of PPIs on *Proteus mirabilis* urease activity

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**Introduction**: Proton pump inhibitors (PPIs) suppress gastric acid by targeting the cysteine residues in H, K- ATPase pumps of gastric parietal cells. Previous studies showed that PPIs exhibit selective inhibitory effect on *H. pylori* urease activity. The aim of this study wasto assessurease activity of *Proteus mirabilis*, as one of the gastrointestinal bacteria, when threated with PPIs.

**Methods**: One *Proteus mirabilis* isolate from a fecal sample was treated with PPIs, Pantoprazole (PAN 128 μg/mL), Lansoprazole (LPZ 8 μg/mL), Omeprazole (OMP 32 μg/mL) that were added to bacterial culture in BHI broth. PPIs were used at MICs that inhibited *H. pylori* urease activity in previous studies. Urease activity of PPIs-treated and untreated *P. mirabilis* was assayed after 24 and 48 hours exposure to PPIs, using Hamilton-Muller protocol with phenol-Hydrochloride reaction. Optical density of the produced $NH_4^+$ at 625 nm was used to determine urease activity.

**Results**: *P. mirabilis* urease activity was dramatically suppressed by PPIs, PAN, LPZ and OMP, showing reduction from 37%, 47% and 73% at 24 hours to 17%, 25% and 26% at 48 hours, respectively. The inhibitory effect was more pronounced after longer exposure time. PAN showed the most inhibitory effect.

**Conclusion**: PPIs inhibitory effect on *H. pylori* urease activity is not selective. Furthermore, similar to *H. pylori* and *P. mirabilis*, PPIs might exert inhibitory effect on urease activity of other bacteria.

F. Siavoshi: None. S. Kadkhodaei: None. A. Hatefi: None.

## P1.45 | Results of the analysis of *Helicobacter pylori* eradication efficiency in the Vinnytsia region (Ukraine)

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Implementation of the Maastricht Consensus (MC-IV) recommendations to overcome H.p. resistance requires a preliminary analysis of the local results effectiveness.

We studied the effectiveness of the eradication schemes used in the Vinnytsia region (Ukraine) during 2008-2018 and their compliance with the recommendations of the MC-IV.

We have analyzed the results of eradication in 571 patients (2008-2018). Depending on the used eradication schemes patients were divided into groups: 376 (65.9%) of patients who were prescribed treatment according to the recommendations of the MC-IV, 195 (34.1%) of patients receiving treatment according to schemes that did not meet the requirements of the MC-IV.

**Results**: Out of 376 patients receiving correct regimens, eradication was achieved in 81.3%. Out of 195 patients receiving inappropriate schemes, eradication was achieved in 76.4%. We have not established a significant difference between groups ($P > 0.05$) regarding the success of eradication depending on compliance with the recommendations of the MC-IV. Among the correct schemes, the most commonly used were panto+clarithro+amoxi (33.4%), panto+clarithro+amoxi+bismuth (12.5%). None of these schemes proved to be significantly more effective compared to the average ($P = 0.64$ and $P = 0.69$, respectively). The choice of PPI used in correct eradication regimens showed a significant prevalence of panto-: 246 cases (65.4%) over ome-, rabe- and eso- (14.8%, 11% 7, 5.31% respectively).

**Conclusions**: A significant proportion of patients (34.1%) received treatment that does not meet valid recommendations. Eradication schemes, even designated according to the recommendations of the MC-IV, revealed a lack of effectiveness (81.3%) in the Vinnytsia region (Ukraine).

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## P1.46 | Comparison of anti- *H. pylori* activity of statins with metronidazole and clarithromycin

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**Background**: Non-antibiotic drugs and vitamins with antibacterial activity might be regarded as effective substitutes in therapeutic

regimens for eradication of refractory bacterial infections. Statins (lipid-lowering drugs) inhibit cholesterol synthesis in human liver. *H. pylori* with cholesterol-rich cell membrane might be affected by statins. In this study, agar dilution method was used to compare anti-*H. pylori* effect of rosuvastatin (RUS), simvastatin (SIM), atorvastatin (ATR) and vitamin C (Vit C) with that of metronidazole(MET) and clarithromycin (CLR).

**Methods**: Five *H. pylori* isolates from gastric biopsy of dyspeptic patients were treated with RUS and SIM (100 μg/mL), ATR (250 μg/mL) Vit C (2048 μg/mL), MET (8 μg/mL) and CLR (2 μg/mL). The used drugs were added to brucella blood agar and *H. pylori* suspension with the turbidity of McFarland No 2 was spot inoculated on the plates. Results were recorded after 7 days microaerobic incubation at 37°C.

**Results**: Out of 5 isolates, one (20%) showed resistance to MET and CLR. However, all the 5 isolates were susceptible to statins and VIT C.

**Conclusions**: Cholesterol in *H. pylori* cell membrane reaches up to 20% and plays an important role in maintaining the integrity and normal permeability of *H. pylori* cell membrane. The inhibitory action of statins on *H. pylori* growth could be due to disruption of cholesterol content in bacterial cell membrane. Drugs such as statins and vit C by disrupting the permeability of bacterial cell envelope could act as antibacterial or enhance the antibiotics efficiency against *H. pylori*.

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## P1.47 | *Helicobacter pylori* eradication strategy according to sequencing-based 23S ribosomal RNA point mutation associated with clarithromycin resistance

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**Background/Aims**: Clarithromycin resistance in *Helicobacter pylori* is associated with point mutations in the 23S ribosomal RNA (rRNA) gene. We investigated the point mutations in the 23S rRNA genes by sequencing and compared the *H. pylori* eradication rates based on the identified clinically significant point mutations.

**Methods**: Sequencing-based detection of point mutations identified four mutations that were considered clinically significant (A2142G, A2142C, A2143G, A2143C), while all the other mutations were considered clinically insignificant. Patients who did not have point mutations or had clinically insignificant point mutations were treated with proton pump inhibitor, amoxicillin, clarithromycin for 7 days, while patients with clinically significant point mutations were treated with proton pump inhibitor, amoxicillin, metronidazole for 7 days. *H. pylori* eradication rates were compared between the two groups.

**Results**: A total of 431 adult patients with *H. pylori* infection were recruited. The clarithromycin resistance rate was 21.3% in the overall group of patients. A2143G was the most clinically significant point mutation (84/431, 19.5%), while T2182C was the most clinically insignificant point mutation (283/431, 65.7%). The *H. pylori* eradication rate in the overall group of patients was 83.7%, and the 7-day PAM-treated clarithromycin-resistance group showed a significantly lower eradication rate than the 7-day PAC-treated nonresistance group [ITT; 55.4% (51/92) vs 74.3% (252/339), $P = 0.001$, PP; 66.2% (51/77) vs 88.4% (252/285), $P = 0.0001$].

**Conclusions**: There were significantly lower eradication rates in the patients with clarithromycin-resistant *H. pylori* as identified by the sequencing of point mutations in the 23S rRNA gene when treated with PAM for 7 days. (NCT03884348)

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## P1.48 | Can metformin inhibit *H. pylori* growth? (in vitro study)

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**Background**: It is still important to find new medicines that can affect *H. pylori* and can inhibit its growth. The aim: to check: can metformin inhibit growth of *H. pylori* in vitro?

**Methods**: We investigate growth of four *H. pylori* strains in presence of metformin in different concentrations. Study have four stages: 1. in a mortar we pound on tablets of two types of metformin (Glucophage 500 mg, Siofor 850 mg). We add 10 mL of the distilled water; 2. in tablet holes for the cultivate of cells we spill the 180 mcl the Brucella broth, 10 mcl bovine serum, then we bring 10 mcl of different strains of *H. pylori* (10*9 cfu/mL) and 10 mcl of metformin in one of its concentration; 3. We stick with a film and incubate at 37 C during 24 hours; 4. We take from each hole the 10 mcl to Petri cups with selective blood culture medium and incubate them in anaerostat at 37 C during 72 hours.

**Results**: We saw that in cultivation of all *H. pylori* strains with metformin in high concentration growth of microorganism was inhibit. Example for *H. pylori* strain 1 is in table.

**Conclusion**: We can see an inhibit activity of metformin in high concentration against *H. pylori* in vitro. New study are needed to check metformin efficacy as antihelicobacter drug in vivo.

| **Inhibit of growth of *H. pylori* strain 1** | |
|---|---|
| Negative control | No growth |
| Positive control | Growth |
| Siofor 1.78 mg/mL | No growth |

| Inhibit of growth of *H. pylori* strain 1 | |
|---|---|
| Siofor 0.178 mg/mL | Growth |
| Siofor 0.0178 mg/mL | Growth |
| Glucophage 1.05 mg/mL | No growth |
| Glucophage 0.105 mg/mL | Growth |
| Glucophage 0.0105 mg/mL | Growth |

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## P1.49 | Risk factors of rebleeding among patients with nonvariceal upper gastrointestinal bleeding with anticoagulant therapy

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**Background and aims**: Acute upper gastrointestinal bleeding (UGIB) is a severe complication associated with oral anticoagulants. However, little is known about the risk factors of rebleeding during anticoagulant therapy. We aimed in this study to evaluate the risk factors of rebleeding after successful endoscopic hemostasis for UGI bleeding in patients taking oral anticoagulants.

**Methods**: Between July 2007 and June 2017, 55 patients with oral anticoagulants were hospitalized due to nonvariceal UGIB and followed up at Korea University Guro hospital. We retrospectively reviewed the clinical characteristics and compared them between patients with and without rebleeding.

**Results**: The most common cause of UGIB was peptic ulcer in 46 patients (83.6%). Rebleeding after hemostasis occurred in 14 patients (25.5%). There were no significant differences between patients with and without rebleeding on age, gender, concomitant medication of antiplatelet or nonsteroidal anti-inflammatory drugs, restart of anticoagulant, *Helicobacter pylori* status, hypotension (systolic blood pressure <90 mm Hg), Hemoglobin, platelet count, INR, BUN and presence of endoscopic stigmata. Univariate analysis revealed that duodenal location (50.0 vs 12.2%, $P = 0.006$) and comorbidities including renal failure, liver disease and malignancy (71.4 vs 28.6%, $P = 0.036$) were significantly different between patients with and without rebleeding. In multivariate analysis, duodenal location (OR 18.7 $P = 0.006$) and comorbidities (OR 8.0, $P = 0.048$) were also significant risk factors for rebleeding.

**Conclusion**: Despite of successful endoscopic hemostasis for UGIB, the rebleeding rate was considerable. Physicians need to be more careful about rebleeding if patients have the duodenal lesion or comorbidities.

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## P1.50 | Bismuth-based vs standard triple therapy for the eradication of *Helicobacter pylori* in Belgium: Preliminary results

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**Background**: *H. pylori* (HP) infection is related to malignant and non-malignant diseases like peptic ulcer, atrophic gastritis and gastric cancer warranting eradication. In Belgium, resistance rates for clarithromycin range between 10 and 15%, being just acceptable for standard triple therapy (STT: 14 days of pantoprazole 40 mg bid, clarithromycin 500 mg bid, amoxicillin 500 mg bid). Since 2015, bismuth-based quadritherapy (BQT: 10 days of bismuth subcitrate 140 mg qid, tetracycline 125 mg qid, metronidazole 125 mg qid, pantoprazole 40 mg bid) became commercially available. The aim of this study is to evaluate the eradication rates (ER) of BQT over STT.

**Methods**: Multicentre, non-blinded randomized, prospective study comparing ER in eradication-naïve HP positive patients. Eradication status is confirmed by urea breath test at least 6 weeks following treatment. Analysis is done by intention to treat (ITT) and per protocol (PP) analysis. Based on estimated ER of 90% for BQT and 75% for STT and 10% loss to follow-up, sample size of 125 patients per group is required.

**Results**: Overall 118 patients were included (STT 60, BQT 58). 9 patients were lost to follow-up (8%). No significant difference in ER between BQT and STT was observed in ITT (83% vs 72%, $P = 0.15$) neither PP analysis (89% vs 78%, $P = 0.13$). No influence of gender or site allocation was observed.

**Conclusion**: Preliminary results show no statistical difference between both groups. However, as the observed eradication rates in PP analysis are in line with the a priori estimation, further inclusion of patients is required to attain sufficient statistical power.

S.A. François: None. S. Kindt: None. F. Mana: None. S. Cadranel: None. P. Bontems: None. V. Lamy: None. R. Ntounda: None. V.Y. Miendje Deyi: None. E. Macken: None.

## P1.51 | Efficacy of levofloxacin-based third-line therapy for the eradication of *Helicobacter pylori* in Seoul

**D. Lee**

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**Backgrounds/Aim**: The seroprevalence of *Helicobacter pylori*(*H. pylori*) in Korea was found to be decreased. But the eradication rates of first- and second-line therapy has been decreasing progressively due

to increased resistance to antibiotics. Therefore there is increasing need for third-line therapy of *H. pylori*. We performed this study to evaluate the efficacy of levofloxacin-based regimens in patients with first- and second-line *H. pylori* eradication failures.

**Methods**: We retrospectively reviewed 16 patients who were treated with third-line therapy in Seoul Paik Hospital between October 2017 and April 2019. Patients, in whom a first-line therapy with proton pump inhibitor(PPI)-clarithromycin-amoxicillin and a second-line therapy with PPI-bismuth-tetracycline-metronidazole had failed, received treatment with lansoprazole (30 mg twice daily), amoxicillin (1 g twice daily) and levofloxacin (500 mg twice daily) for 10 days. Eradication rates were confirmed with urea breath test 4 weeks after the cessation of therapy.

**Results**: A total of 16 subjects (Male : Female = 6 : 10, Age : 48-75 years old, Median age : 66.5 years old) were enrolled in the study. All patients took all the medications correctly. *H. pylori* eradication rates were 43.8% (7 of 16) in the levofloxacin-based regimen.

**Conclusions**: *H. pylori* eradication rates of levofloxacin-based regimen could not achieve enough eradication rate in this study. Also, a recent study of 14 people who failed to treat first- and second-line therapy showed 57.1% rate of eradication in Korea. Since the eradication rate of third-line therapy including levofloxacin is low, nationwide multicenter studies on eradication therapy strategies including new drugs such as potassium-competitive acid blocker will be needed.

D. Lee: None.

## P1.52 | Efficacy of levofloxacin-based third-line therapy for the eradication of *Helicobacter pylori* in central Seoul, Korea

**J. Moon**[1]; D. Lee[1]; Y. Shin[1]; S. Lee[1]; T. Park[1]; S. Ryu[1]; Y. Kim[1]; S. Seol[2]

[1]*Inje University Seoul Paik Hospital, Seoul, Republic of Korea;* [2]*Inje University Busan Paik Hospital, Busan, Republic of Korea*

**Backgrounds/Aim**: The seroprevalence of *Helicobacter pylori*(*H. pylori*) in Korea was found to be decreased. But the eradication rates of first and second-line therapy has been decreasing progressively. Therefore there is increasing need for third-line therapy of *H. pylori*. We performed this study to evaluate the efficacy of levofloxacin-based regimens in patients with first and second-line *H. pylori* eradication failures.

**Methods**: We retrospectively reviewed 16 patients who were treated with third-line therapy in Seoul Paik Hospital located in central Seoul, Korea between October 2017 and April 2019. Patients, in whom a first-line therapy with proton pump inhibitor (PPI)-clarithromycin-amoxicillin and a second-line therapy with PPI-bismuth-tetracycline-metronidazole had failed, received treatment with lansoprazole (30 mg twice daily), amoxicillin (1 g twice daily) and levofloxacin (500 mg twice daily) for 10 days. Eradication rates were confirmed with urea breath test 4 weeks after the cessation of therapy.

**Results**: A total of 16 subjects (Male : Female = 6 : 10, Age : 48~75 years old, Median age : 66.5 years old) were enrolled in the study. All patients took all the medications correctly. *H. pylori* eradication rates were 43.8% (7 of 16) in the levofloxacin-based regimen.

**Conclusion**: *H. pylori* eradication rates of levofloxacin-based regimen could not achieve enough eradication rate in this study. Also, a recent other study showed 57.1% rate of eradication in Korea. Since the eradication rates of levofloxacin-based third-line therapy is low, nationwide multicenter studies on eradication therapy including new drugs such as potassium-competitive acid blocker will be needed.

J. Moon: None. D. Lee: None. Y. Shin: None. S. Lee: None. T. Park: None. S. Ryu: None. Y. Kim: None. S. Seol: None.

# POSTER ROUND 1.2 DRUG RESISTANCE AND CLINICAL ISSUES

## P1.53 | Whole Genome Sequencing analysis for characterization of genomic variations associated with antimicrobial resistance among Greek *Helicobacter pylori* isolates

G. Papadopoulou[1,2]; **B. Martinez-Gonzalez**[1]; T. Karamitros[1]; P. Kollia[2]; A. F. Mentis[1]; D. N. Sgouras[1]

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We have applied a Whole Genome Sequencing (WGS) approach for the identification of genomic variations contributing to clarithromycin ($CLA^R$) and metronidazole ($MET^R$) resistance among *Helicobacter pylori* (*Hp*) isolates. We included in the study *Hp* clinical strains isolated from adult symptomatic patients, previously characterized for phenotypic susceptibility using the E-test (sensitive n = 11, $CLA^R$ n = 9, $MET^R$ n = 14, $CLA^R$-$MET^R$ n = 3). Data were generated using the Ion Torrent S5 platform and contig-sequences were *de novo* assembled. Gene-based and single nucleotide polymorphism (SNP) bioinformatic analysis was performed using standard BLAST tools, in genes related with $CLA^R$ (*23S rRNA*) and $MET^R$ (*rdxA*, *frxA*, *rpsU*). $CLA^R$-associated mutation A2146G (n = 5) was observed uniquely in the $CLA^R$ group, whereas A2147G was observed both in the $CLA^R$ (n = 2) and in the $CLA^R$-$MET^R$ group (n = 2). Absence of these mutations was identified in 2 $CLA^R$ and one $CLA^R$-$MET^R$ isolates, necessitating further validation in phenotypic susceptibility. T2186C transition previously associated with $CLA^R$ was identified in 2 $CLA^R$ and one susceptible strain. Eighty-one SNPs were identified in *23S rRNA* gene with reference to 26695 strain, n = 35 of which uniquely in sensitive strains,

n = 17 in CLA$^R$ and n = 29 in both groups. MET$^R$-associated mutations Q6H, T31E, R90K, A118T and V172I were identified in *rdxA* gene of 15/17 MET$^R$ and 16/20 sensitive strains, while R131K was predominantly observed in MET$^R$ strains ($P$ = 0.038*). Premature stop codon (n = 3) and frame-shift mutations (n = 3) in *rdxA* gene were observed in MET$^R$ isolates. Further validation and gene target analysis is required to assess WGS contribution in the investigation of antibiotic resistance mechanisms.

G. Papadopoulou: None. B. Martinez-Gonzalez: None. T. Karamitros: None. P. Kollia: None. A.F. Mentis: None. D.N. Sgouras: None.

## P1.54 | Prevalence of multidrug resistance rate of *Helicobacter pylori* in Korea: Nationwide multicenter study

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**Background and aim**: We aimed to evaluate the prevalence of multidrug resistance (MDR) of *Helicobacter pylori* in Korea.

**Methods**: Five hundred and ninety adult subjects were prospectively enrolled from 2017 to 2018 from 15 centers. The agar dilution method was used to determine the minimum inhibitory concentration of amoxicillin, clarithromycin, metronidazole, tetracycline, ciprofloxacin, and levofloxacin for each *H. pylori* isolate.

**Results**: The culture success rate was 60.2% (349/580). Resistance rates against clarithromycin, metronidazole, amoxicillin, tetracycline, levofloxacin, and ciprofloxacin were 17.8%, 29.5%, 9.5%, 0%, 37.0%, and 37.0%, respectively. The *H. pylori* with MDR rate was 25.2% (88/349) among amoxicillin, clarithromycin, metronidazole, tetracycline, and quinolone, and 11.2% (39/349) among four of these major antibiotics except for quinolone. There were 60, 23, and 5 subjects who had a 2, 3, and 4 antibiotic-resistant *H. pylori* profile, respectively (29.1%, 11.2%, and 2.4% of the *H. pylori* antibiotic resistant subjects, respectively). There were 15/62 subjects showing amoxicillin- clarithromycin (24.2%) and 25/62 showing metronidazole-clarithromycin (40.3%) co-resistance to *H. pylori*. Cases of *H. pylori* resistance to clarithromycin had a 53.2% probability of an MDR with amoxicillin or metronidazole. Simulated success rate of empirical primary standard PCA and rescue PBMT treatment were 77% and 61%, respectively with 349 subjects. Simulated success rate of empirical primary PMA and concomitant treatment were 65% and 89%, respectively.

**Conclusion**: *H. pylori* with MDR rate for major four antibiotics was as high as 11.2%. 40.3% and 24.2% of subjects with clarithromycin resistance also showed metronidazole and amoxicillin resistance.

C. Kee Don: None. J. Kim: None.

## P1.55 | Multicenter survey of antimicrobial resistance in *Helicobacter pylori* isolates in Greece - Trends of resistance 1998-2018

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Resistance to antibiotics among *Helicobacter pylori* (*Hp*) isolates is a matter of concern worldwide due to important implications in treatment failures. In this surveillance study carried out from December 2018 to January 2019, we estimated primary resistance to clarithromycin (CLA), metronidazole (MET), levofloxacin (LEV), amoxicillin (AMO), tetracycline (TET) and rifabutin (RIF) of 50 isolates from Greek adult patients. Data were prospectively correlated with similar surveys carried out 10 and 20 years ago. Antibiotic susceptibility was assessed by E-test method. Primary resistant rates were 40% (20/50) for MET, 28% (14/50) for CLA and 8% (4/50) for LEV. No resistance was observed for AMO, TET and RIF. Antibiotic resistant rates were significantly higher for MET and CLA when compared to results of a similar survey undertaken in 1998 (33.3% for MET and 2.3% for CLA-resistance), but not quite significant when compared with a survey carried out 10 years ago (2008-2009: 35.3% for MET, 24.7% for CLA and 7% for LEV-resistance). Over the last 20 years, consumption of antibiotics, particularly of macrolides in the Greek population, has increased resulting to a parallel dramatic rise in CLA-resistant *Hp* isolates. Since the latest European antimicrobial-susceptibility survey, ten years ago, resistance to MET, CLA and LEV remains relatively stable. It is important to note however, that increased levels of MET and CLA-resistance require that professionals must exercise caution when using these agents for empirical treatment, if local antimicrobial resistance patterns are not available. Timely surveillance programs will be essential components for efforts to combat *Hp* resistance.

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## P1.56 | Expression of efflux pump gene hefA, hefD and hefG in clinical isolated *Helicobacter pylori* strains

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**Background and Objective**: Efflux pump gene hefA, hefD and hefG encode protein that compose the outer membrane channel protein of efflux pump which were important for antibiotic resistance. The aim of this research was to explore the expression of efflux pump gene hefA, hefD and hefG in clinical isolated *Helicobacter pylori* strains.

**Materials and methods**: 26 *H. pylori* strains were selected to detect gene expression, including 5 multi-drug resistance (MDR) strains, 6 single metronidazole resistance strains, 5 single levofloxacin resistance strains, 2 single clarithromycin resistance strains and 8 strains that were susceptibility to all antibiotic that were widely used in anti-*H. pylori* treatments. The gene expression of hefA, hefD and hefG were measured with qRT-PCR.

**Results**: The gene expression of hefA and hefD were significant higher in MDR strains when compared with any other groups ($P < 0.05$). While the expression of hefG did not show significant difference among these groups ($P > 0.05$). There was no significant difference when compared the efflux pump gene expression between susceptibility group with single resistance groups, respectively.

**Conclusion**: hefA and hefD expression were important for the MDR strain, hefG may play a different role compare to hefA and hefD. There was no significant difference when compared the expression of hefA, hefD and hefG between susceptibility group and single resistance group.

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## P1.57 | Prevalence of primary and secondary antimicrobial resistance of *Helicobacter pylori* isolates in Korea

**E. Gong**[1]; H. Na[2]; J. Ahn[2]; J. Lee[2]; K. Choi[2]; K. Jung[2]; D. Kim[2]; H. Song[2]; G. Lee[2]; H. Jung[2]

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**Background**: Antimicrobial resistance significantly affects the efficacy of eradication therapy in patients with *H. pylori* infection.

**Methods**: Primary and secondary antimicrobial resistances were investigated in *H. pylori* isolates from 377 patients without any history of eradication therapy and 141 patients following failure of eradication therapy. Minimum inhibitory concentration (MIC) values and resistance rates to 6 antibiotics were assessed using the serial two-fold agar dilution method. Heteroresistance was evaluated in 213 patients in whom a pair of biopsy specimens were obtained from both the antrum and corpus of the stomach.

**Results**: Primary resistance to amoxicillin, clarithromycin, metronidazole, tetracycline, levofloxacin, and ciprofloxacin was found in 9.0%, 24.4%, 31.0%, 0%, 37.1%, and 36.6% of isolates. Secondary resistance rates were 23.4%, 85.1%, 62.1%, 0%, 49.6%, and 50.4%, respectively. Regarding multidrug resistance, 42.4% (160/377) of the primary isolates and 78.0% (110/141) of the secondary isolates had resistance to two or more antibiotics. The MIC values of the secondary isolates showed a shift to higher concentrations compared with those of the primary isolates. Heteroresistance was observed in 19.2% (41/213) of isolates, and it seemed to be less frequent in the secondary isolates (14.3%) than in the primary isolates (21.7%).

**Conclusions**: The MIC values after antibiotic exposure were higher than those of the primary isolates. Antimicrobial heteroresistance of *H. pylori* may be one of the causes of eradication failure.

**Key words**: *Helicobacter pylori*; antibiotic resistance; Mixed infections

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## P1.58 | Prevalence of *Helicobacter pylori* clarithromycin resistance in Central Hungary

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**Background**: Decreasing eradication rates of *Helicobacter pylori* (*H. pylori*) infections has been observed worldwide. Clarithromycin (Cla) is one of the most important eradication antibiotics and the development of resistance against this can contribute to the increasing rate of unsuccessful eradications.

**Materials and Methods**: Gastric biopsy specimens of 6800 *H. pylori* infected patients were investigated by a rRNA-targeted Cla-resistance FISH method as reflex test for the *H. pylori* positive cases of the clinics of Semmelweis University, Budapest and five further hospitals from Central Hungary. Prevalence of Cla-resistant cases were analysed from the 2004-2018 period.

**Results**: Overall *H. pylori* Cla-resistance rate was 18.3%. By analyzing the different sub-periods, prevalence of Cla-resistance initially decreased but an increasing tendency was observed from 2013: 18.4% (2004-2006); 16.5% (2007-2009); 16.6% (2010-2012); 19.5%

(2013-2015); 22.7% (2016-2018). Significant difference ($P < 0.01$) was observed in the resistance rates between university clinics (20.2%) and other hospitals (17.3%) as well as between male (15.4%) and female (20.5%) patients.

**Conclusion**: Considering the increasing prevalence of Cla-resistance, use of clarithromycin in *H. pylori* eradication is not recommended without susceptibility testing in the Central Hungarian region.

É. Kocsmár: None. I. Kocsmár: None. G. Buzás: None. I. Hritz: None. A. Szijártó: None. G. Lotz: None.

## P1.59 | Knockout RND efflux pump gene could prevent the occurrence of antibiotic resistance gene mutation

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**Aims**: The aim of this study was to investigate whether knockout efflux pump gene hefA, hefD or hefG of *Helicobacter pylori* could prevent the occurrence of antibiotic resistance gene mutation.

**Material**: *H. pylori* strain 26695 were used to knockout gene hefA, hefD and hefG, respectively. The wild type strain 26695 and its mutant strain 26695_ΔhefA, 26695_ΔhefD and 26695_ΔhefG were exposed to discontinuous elevation of antibiotic dose based on their original minimum inhibitory concentration (MIC). The occurrence of point mutation in target genes was determined by PCR and sequencing.

**Results**: In the process of developing clarithromycin resistance, strain 26695 detect A2142C mutation of 23S rRNA gene in the stage of 1*MIC concentration, 26695_ΔhefD and 26695_ΔhefG detect A2142G mutation in the stage of ½*MIC, strain 26695_ΔhefA detect A2142G mutation in the stage of 4*MIC. In the process of developing levofloxacin resistance, strain 26695 could detect D91N mutation of gyrA gene in the stage of 2*MIC concentration, 26695_ΔhefD and 26695_ΔhefG detect D91G mutation in the stage of 2*MIC, 26695_ΔhefA detect D91N mutation in the stage of 32*MIC. In the process of developing metronidazole resistance, strain 26695 detect T49K mutation of rdxA gene in the stage of 4*MIC concentration, 26695_ΔhefD detect T49K mutation in the stage of 8*MIC concentration and 26695_ΔhefG detect nonsense mutation in the stage of 16*MIC, knockout strain 26695_ΔhefA didn't detect any mutation in the process.

**Conclusion**: Knockout hefA gene of *H. pylori* could delay or prevent the occurrence of antibiotic resistance gene mutation in the process of developing antibiotic resistance.

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## P1.60 | Knockout RND efflux pump gene may reverse antibiotic resistance in *Helicobacter pylori*

**Y. Wang**[1]; L. Yan[2]; Y. An[2]; Y. Wang[2]; Q. Zhao[1]; R. Zhao[1]; S. Wu[1]; Y. He[1]; Y. Song[1]; Y. Xie[1]

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**Aims**: The aim of this study was to investigate whether knockout efflux pump gene hefA, hefD or hefG of *H. pylori* could reduce susceptibility to antibiotic or reverse the occurrence of antibiotic resistance gene mutation.

**Material**: Several clinical *H. pylori* strains were used to construct hefA, hefD or hefG knockout strain, including 3 multiple drug resistance (MDR) strains, 2 mono-clarithromycin resistance strains, 2 mono-levofloxacin strains and 1 mono-metronidazole resistance stain. The minimum inhibitory concentration (MIC) before and after efflux pump gene knockout were detected with E-test method. The sequence of target genes was detected by PCR and sequencing.

**Results**: For these three MDR strains, the MIC of clarithromycin and levofloxacin didn't decrease more than four times, nor did the mutations of 23SrRNA or gyrA that related to clarithromycin and levofloxacin resistance been reversed. But one of these MDR strains showed significant decrease for the MIC of metronidazole, and the sequence of rdxA gene also changed when hefA hefD, and hefG gene were knockout respectively. For these two clarithromycin resistance strains, the MIC decrease more than four time when hefA or hefD were knockout respectively, but the mutation of 23SrRNA still there. For these two levofloxacin resistance strains, their MIC or point mutation of gyrA didn't change a lot. For the metronidazole resistance strain, Its MIC decreased and the point mutation of rdxA changed.

**Conclusion**: Knockout efflux pump gene hefA or hefD of *H. pylori* may reduce it susceptibility to clarithromycin and metronidazole for some resistance strains, but not for levofloxacin.

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## P1.61 | Detection of clarithromycin resistance in *Helicobacter pylori* with whole genome sequencing and a webtool

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**Background**: *H. pylori* is a Gram negative, microaerophilic bacterium that represents a key factor in various gastroduodenal diseases. Antibiotic susceptibility still mainly relies on culture and drug susceptibility testing that is time consuming and can be uncertain. However, resistance detection by whole genome sequencing (WGS) or molecular assays targeting point mutations in specific genes

offers a more precise method. Our aim is to provide a webtool for an easy way to detect resistance by analysis of WGS data.

**Method**: In 346 biopsies collected from Danish patients with an indication for gastroscopy (January 2017- ongoing), 13% were found positive for *H. pylori* by PCR. Out of 350 biopsies 6% were found positive by cultivation. Culturable strains (N = 19) were WGS and the data analyzed for clarithromycin resistance with a webtool designed to detect mutations in the 23srRNA gene (A2142C, A2142G, A2143G, A2144G, T2182C, C2244T, T2712C). The results were compared with E-testing results.

**Results and conclusion**: Susceptibility testing of 19 *H. pylori* strains found one resistant strain while analysis of WGS data revealed 6 strains with mutations in the 23srRNA gene: 21% (T2182C), 5.2% (A2143G) and 5.2% (C2244T). 22.2% of the PCR positive biopsies were infected with both susceptible and resistant strains. The webtool provides fast and easy analysis of WGS data from *H. pylori* strains. Quality assessment of the webtool will be done using *H. pylori* strains with known clarithromycin resistance and we are working on expanding the webtool to include detection of rifampicin resistance. More analysis will be completed.

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## P1.62 | MALDI-TOF-MS as tool to identify clarithromycin-resistant *H. pylori* isolates in Gipuzkoa, Spain

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**Introduction**: Clarithromycin resistance (CLA-R) is the main reason for failure of *Helicobacter pylori* infection treatment. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF-MS) is a rapid methodology for bacteria identification. New clinical applications of MALDI-TOF-MS in the field of microbiology are nowadays addressed as the discovery of new biomarkers for antimicrobial resistance detection.

**Aim**: To evaluate the potential of MALDI-TOF-MS for identification of CLA-resistant *H. pylori* isolates.

**Methods**: All *H. pylori* strains used in the experiment were characterized by sequencing. Bacterial proteins were extracted using the ethanol/formic acid method according to Bruker Daltonics protocol. A mass spectra library was constructed by analyzing 9 CLA-Resistant and 9 CLA-Sensitive *H. pylori* isolates with five spectra per sample. Raw data generated with MALDI-TOF-MS were preprocessed using FLEX analysis software (smoothing and baseline subtraction). The spectra were further analyzed (intra- and inter-label Biomarker discovery analysis and Principal Component Analysis (PCA) using Mass-Up v1.0.13 open software.

**Results**: *H. pylori* showed a high variability at inter strain level. There were eleven peaks present in most of the strains either sensitive or resistant (table). The inter-label analysis did not show any discriminative biomarker ($q$-value > 0.05). PCA evaluation set formed a heterogeneous group with no clustering.

**Conclusion**: In our experience MALDI-TOF-MS could not differ between clarithromycin-sensitive and clarithromycin-resistant *H. pylori* strains.

| Peak (m/z) | R1 | R2 | R3 | R3 | R4 | R5 | R6 | R7 | R8 | R9 | S1 | S2 | S3 | S4 | S5 | S6 | S7 | S8 | S9 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2,157 | | | | | | | nd | | | | | | | | | | | | |
| 2,621 | | | | | | | | | | | | nd | | | | | | | |
| 2,756 | | | nd | | | | | nd | | | | | | | | | | nd | nd |
| 3,031 | | | | | nd | | | | | | | nd | | | | nd | nd | nd | |
| 3,563 | nd | | | | | | | | nd | | | | | | | | | nd | |
| 4,321 | | | | | | | nd | | | | | | | | | | | | |
| 4,485 | nd | | | | | | | | | nd | | | | | | | nd | | |
| 5,247 | | | | | | | | | | | | | nd | | | | | | |
| 6,067 | | | | | | | | | | | | | | | | | | nd | |
| 7,129 | nd | | | | | | | | nd | | | | | | | | | nd | |
| 9,097 | | | | | | | nd | | | | nd | nd | nd | | | | nd | nd | |

Empty square: detected, nd: no detected, R: Resistant, S: Sensitive.

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## P1.63 | Primary and secondary *Helicobacter pylori* resistance among Serbian adult population

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**Introduction**: Antibiotic resistance is the most important factor leading to the failure of eradication rate. Our study aimed to focus on the prevalence of *Helicobacter pylori* primary and secondary antibiotic resistance in Serbia.

**Methods**: *Helicobacter pylori* was cultured from biopsies that were collected from patients and the antimicrobial susceptibility of *Helicobacter pylori* was determined using the E-test (clarithromycin, amoxicillin, tetracycline, metronidazole and levofloxacin) according to the EUCAST guideline. Point mutations in the 23s rRNA gene of clarithromycin-resistant strains and main mutation for gyrA gene of quinolones-resistant strains were investigated using real-time PCR.

**Results**: From total of 128 patients 35.2% (45/128) originated from patients who had never been treated for *Helicobacter pylori* infection, while the remaining 83 were isolated from patients with two or more previous eradications (64.8%). Main results with primary, secondary and overall resistance rate were shown in Table 1.

**Conclusion**: Thus, the high resistance to Metronidazole and Clarithromycin asks the question for using these drugs in eradication of *H. pylori* infection without culture and antibiogram. Commitment to quadruple therapy, for 14 days, as the first choice for eradication is required by a consensus. High level of secondary resistance compared to primary, shows inconsistent implementation of international and national consensus in real-life praxis. The perspective of personalized therapy based on culture and/or PCR molecular test is imposed as a possible future solution.

**TABLE 1**

| AB Resistance | Total | Primary | Secondary | *P* |
|---|---|---|---|---|
| Amoxicilin | 20.3% | 4.4% | 28.9% | <0.001 |
| Clarithromycin | 45.3% | 26.7% | 55.4% | <0.001 |
| Metronidazole | 60.2% | 38.5% | 67.5% | 0.002 |
| Fluoroquinolones | 16.4% | 13.3% | 18.1% | 0.3 |
| Tetracycline | 12.3% | 3.4% | 15.5% | <0.001 |
| CLA+MET | 27.9% | | | |

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## P1.64 | The primary resistance of *H. pylori* strains from South-Western Polish pediatric and adult patients in 2016-2018

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**Introduction**: Increased *H. pylori* resistance to currently used antibiotics is a global problem. Monitoring the antibiotic resistance of this bacterium is an important step in creating effective strategies for *H. pylori* control.

**Aim**: To assess the prevalence of antimicrobial resistance of *H. pylori* strains isolated from pediatric and adult patients with primary infections.

**Methods**: Antral biopsies from 334 patients (180 children and 154 adults) were obtained. A total of 71 clinical *H. pylori* strains (34 from children and 41 from adults) were isolated and examined for amoxicillin (AMX), clarithromycin (CLR), metronidazole (MTZ), tetracycline (TET) and levofloxacin (LEV) susceptibility. The activity of antibiotics was measured by E-tests. Strains were considered as resistant to antibiotics with minimum inhibitory concentrations (MICs) counted for ≥ 0.125 μg/mL (AMX), ≥0.5 μg/mL (CLR), ≥8 μg/mL (MTZ), and ≥ 1 μg/mL (TET and LEV).

**Results**: The highest prevalence of antibiotic resistance in *H. pylori* strains was observed for CLR and MTZ, counting for 56% and 41% vs 26.8% and 43.9% for children and adults, respectively. A much lower frequency of isolation of resistant strains was demonstrated for TET and LEV, being 2.9% and 18% vs 2.4% and 17% for pediatric and adult patients, respectively. The presence of AMX-resistant strains was not observed.

**Conclusion**: The *H. pylori* strains isolated from patients with primary infections showed a high level of antibiotic resistance to both CLR and MTZ. The prevalence of CLR-resistant strains is twice as high in children compared with adults.

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## P1.65 | Antimicrobial stewardship and *Helicobacter pylori*: A new beginning

**D. Y. Graham**

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*H. pylori* required more than 20 years before it was accepted as an infectious rather than a gastroenterology disease. Originally therapy was developed by trial and error as if cure was impossible and

there was a placebo response (i.e., as a GI diseases such as constipation). Successful regimens, defined as cure ≥95% of susceptible infections in adherent subjects, were developed but were continued even after antimicrobial resistance had greatly reduced their effectiveness. Antimicrobial stewardship one uses only drugs for which the infection is susceptible, at optimum dose, formulation, dosing interval, dosing frequency, and duration. Infectious disease therapies typically achieve close to 100% cures and comparative trials use non-inferiority trial designs in which both regimens achieve high cure rates. In contrast, traditional *H. pylori* trials often used an ineffective regimen with unoptimized antibiotic combinations. Consents are uninformed when patients are denied knowledge that one comparator is known to be no longer effective. Meta-analyses combine studies with different drugs, drug combinations, and treatment durations in populations often with high and unmeasured resistance and declare better of two very poor results a winner. Treatment regimens (drugs, doses, durations) have been defined by Pharma rather than by results. Now that *H. pylori* has been defined as an infectious disease, we face new challenges including re-education of clinicians and investigators regarding the established infectious disease treatment paradigms. Following the well-established trail blazed by the infectious disease community we can change from enriching Pharma and their speakers and get about curing patients and eliminating disease.

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## P1.66 | The comparison of new and classical point mutations associated with clarithromycin resistance in *Helicobacter pylori* strains isolated from dyspeptic patients and their effects on phenotypic clarithromycin resistance

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We aimed to investigate the presence of three recently identified point mutations (A2115G, G2141A, and A2144T) and compare them with classical most encountered three point mutations (A2142G, A2142C A2143G) in *H. pylori* strains in Turkey.

A total of 63 patients with a mean of age as 47,079 were included. The E-test method (for clarithromycin) was used for the clarithromycin antimicrobial susceptibility test of isolated *H. pylori* strains. Real-time PCR method was used for the detection of point mutations.

A total of 24 *H. pylori* strains were detected as clarithromycin resistant (38.1%) (> 0.5 mg/L). In the phenotypically clarithromycin-resistant strains (n:24), the new A2115G, A2144T, and G2141A and the classical A21425G and A2143G point mutations were detected in 6 (25%), 7 (29.1%), 8 (33.3%), 8 (33.3%) and 11 (45.8%) of the clarithromycin resistant strains *H. pylori* strains, respectively. The A2144T point mutation had the highest median MIC value as 3 mg/L amongst the new mutations. Classical mutations (A2142G and A2143G) indicated the highest median MIC values (256) compared with the new mutations. The presence of the A2115G (OR:31.66), A2144T (OR:36.92), and G2141A (OR:28.16) mutations increased the likelihood of clarithromycin resistance in *H. pylori* strains by 31.66-, 36.92-, and 28.16-folds (ORs) according to the binary logistic regression analysis.

We could only make a suggestion by considering the median MIC values as classical mutations were resulted in high clarithromycin MIC values compared than new mutations. These new point mutations likely only moderately impact clarithromycin-resistant in *H. pylori* strains.

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## P1.67 | Point mutations in the development of antibiotic resistance in *Helicobacter pylori*

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**Aims**: The aim of study was to determine the change of point mutations in the development of antibiotic resistance in *H. pylori*.

**Methods**: Seven *H. pylori* strains were exposed to discontinuous elevation of antibiotic dose, respectively. The occurrence of certain point mutation in target genes was determined by PCR and sequence.

**Results**: Six strains successfully develop to clarithromycin resistance status, A2143G act as first mutation were found in four strains, two of these four strains transfer to A2142G in further developing process, A2142C and A2142G were found in other two strain, respectively. Seven strains develop to levofloxacin resistance. Mutations at Asn-87 and Asp-91 of gyrA could found in all strains, Asp-91 mutation act as first mutation in six strains, Asn-87 and Asp-91 double mutation of gyrA were found in seven strain after the whole development process. These point mutations including D91N, D91G, D91Y, N87K. seven strains develop to metronidazole resistance, the point mutation of rdxA have huge variation among different strains and difference development stages, one strain showed no mutation of rdxA gene in the whole process.

**Conclusion**: Gene mutations of 23SrRNA, gyrA were key factors associated with clarithromycin and levofloxacin of *H. pylori*. A2143G of

23SrRNA were the major mutation in the development of clarithromycin resistance, strain with this mutation could transfer to A2142G in further stimulated with clarithromycin. Mutations at Asn-87 and Asp-91 of gyrA were the main change in the develop of levofloxacin resistance. There were huge variations in rdxA mutation in the develop of metronidazole resistance.

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## P1.68 | The prevalence of single and multidrug antibiotic resistance in *Helicobacter pylori* isolated from Iranian dyspeptic patients

B. Attaran[1]; B. Ghadiri[1]; S. Kalateh[1]; N. Eskini[1]; R. Azimi[1]; M. Esmaeili[1]; M. Tashakoripoor[2]; M. Eshagh Hosseini[2]; **M. Mohammadi**[1]

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**Background**: Antibiotic resistance is an ever-rising dilemma regarding the efficiency of *Helicobacter pylori* eradication. In parallel, multi-drug resistant (MDR) phenotypes have become a global health concern. Here, we have evaluated the prevalence of single and multidrug antibacterial resistance, against four commonly prescribed antibiotics.

**Methods**: Gastric biopsies, from dyspeptic patients (n = 300) having referred for gastroscopy, at Amiralam Hospital (Tehran, Iran), were cultured. These subjects constituted of 68% (75/110) NUD and 32% (35/110) PUD patients. Of these, 110 *H. pylori* isolates were obtained and underwent antibiotic (levofloxacin, clarithromycin, amoxicillin, and tetracycline) susceptibility testing, by Epsilometer-test, using EUCAST break points. These isolates were thus, categorized according to the combination of antibiotic resistance.

**Results**: The obtained *H. pylori* isolates (n = 110) were categorized into five groups: (A) susceptible to all 4 tested antibiotics (55/110, 50%), (B) single resistance to *1* of the tested drugs (31/110, ~28%), (C) double resistance to *2* of the tested drugs (13/110, ~12%), (D) triple resistance to 3 of the tested drugs (10/110, ~9%), (E) quadruple resistance to all 4 tested antibiotics (1/110, ~1%). Taken together, half (55/110, 50%) of the strains were resistant to at least one antibiotic. Taken separately, ~8% (9/110), ~16% (18/110), ~28% (31/110), and 31% (34/110) of the *H. pylori* isolates, collected from our dyspeptic population, were resistant to amoxicillin, clarithromycin, tetracycline and levofloxacin, respectively.

**Conclusion**: These results indicate an alarming frequency of multidrug resistant (MDR) *H. pylori* isolates, infecting adult Iranian dyspeptic patients and call for closer clinical surveillance and caution in prescribing eradication regimens.

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## P1.69 | Current resistance rate of *Helicobacter pylori* with Standard Triple Therapy in Libyan Dyspeptic Patients: - Preliminary results

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**Background**: *Helicobacter pylori* (*H. pylori*) is a common globally distributed gastric pathogen. In developing countries, antimicrobial resistance rate in *H. pylori* is widespread. Currently, there are no data regarding the efficacy of First -Line Therapy in Libya.

**Aims**: To assess the resistance rates for *H. pylori* against the Standard Triple Therapy in an Libyan cohort.

**Materials & Methods**: We studied Seventy - Five dyspeptic patients, (35) children & (22) adults, who infected with *H. pylori* diagnosed by Histology. The dyspeptic patients were randomized to receive the recommended first- line *H. pylori* treatment for 14 days. Eradication was assessed by The Ammonia Breath Test (Helic- test, Association of Medicine and Analytic, St-Petersburg) 4 - 5 weeks following completion of therapy.

**Results**: Among the adults (16 females, 6 males, median age 48 years). Three patients (13.6%) who failed first line therapy were cured by quadruple therapy (PPI + Pylera Capsule). However, with dyspeptic children (25 females, 10 males, median age 10 years) there were seven patients (20%) failed with the triple therapy and cured by (PPI+ Amo+ Met).

**Conclusion**: In Libya. For the adult dyspeptic patients who failed standard eradicating treatment, the use of quadruple therapy can be authorized as a first line eradication regimen. However, in our paediatric dyspeptic patients, *H. pylori* antibiogram should be granted in order to improving treatment outcomes. For children & adult dyspeptic patients it is recommended continuous surveillance of resistance rates be undertaken to optimize the *H. pylori* treatment.

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## P1.70 | Response to triple standard therapy > eradication of infection with *Helicobacter pylori* in a center of north-eastern Romania

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**Introduction**: *Helicobacter pylori* infection is one of the most widespread in the world. The Maastricht V consensus recommends the

treatment of all patients infected with *Helicobacter pylori*. The abusive use of antibiotics > other pathologies (respiratory, urinary)has increased bacterial resistance.

Aims: Evaluation of the response to triple standard therapy > the eradication of *Helicobacter pylori* in a gastroenterology center in northeastern Romania. Another endpoint was the indirect assessment of clarithromycin resistance in this area.

**Material & method**: We included 113 patients admitted to the Gastroenterology Department of Bacau County Emergency Hospital during 01 January to 31 December 2018, who were found with *Helicobacter pylori* infection by determining the stool antigen test. All patients received treatment eradication according to the scheme: every 12 hours IPP+ Amoxicillin 1 gram every 12 hours+Clarithromycin 500 mg every 12 hours, 14 days. Treatment response was performed 2 months after the end of treatment by testing the stool antigen. Upper digestive endoscopy has been performed in patients with risk factors.

**Results**: Eradication of *Helicobacter pylori* infection was documented in 91(80%) patients, most of them were women(63%), from urban area(69%), mean age 65 ± 10.5 years. In 22(19%) cases, the elimination of infection was not achieved. The most common endoscopic lesion was chronic antral gastritis(36% <55% respectively).

**Conclusions**: The low eradication rate raises suspicion of resistance to clarithromycin in the northeastern region of Romania. There were no significant demographic differences between patients the two groups. Performing the susceptibility test > clarithromycin by antibiogram after gastric biopsy < culture would be a therapy-effective solution.

E.V. Popovici: None.

## POSTER ROUND 2.1 HELICOBACTER AND EXTRAGASTRODUODENAL DISEASE

### P2.01 | Influence of *Helicobacter pylori* infection and atrophic gastritis on the gut microbiota in a Japanese population

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**Background**: Although infection with *Helicobacter pylori* and subsequent atrophic gastritis modulate the gastric conditions, their relationship with the gut microbiota in Japanese population have not been clearly characterized.

**Methods**: A cohort of 1123 subjects who participated in a health survey were studied. Infection of *H. pylori* was defined by both serum antibody and stool antigen test. The presence and severity of atrophic gastritis were defined by serum levels of pepsinogens. The relative abundance of each bacterial species in fecal samples was calculated by using 16S ribosomal RNA amplification, and the composition ratios of bacterial taxa were evaluated using propensity score matching.

**Results**: The abundance of three orders, four families, and four genera were significantly higher in *H. pylori*-infected subjects than in non-infected subjects (FDR < 0.05). In *H. pylori*-infected subjects with severe atrophic gastritis, the abundance of the class *Bacilli*, order *Lactobacillales*, family *Streptococcaceae*, and genus *Streptococcus* was significantly higher than that in *H. pylori*-infected subjects without atrophic gastritis (FDR < 0.05).

**Conclusions**: A significant increase in the relative abundance of several taxa was observed in gut microbiota of Japanese subjects with *H. pylori* infection. Among the subjects with severe atrophic gastritis, the increase in the genus *Streptococcus* is a remarkable characteristic.

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### P2.02 | Development of endoscopic scoring system to predict risk of intestinal type gastric cancer: Preliminary prospective study

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**Background/Aims**: We aimed to develop endoscopic scoring system to evaluate atrophic gastritis and intestinal metaplasia using narrowing band imaging (NBI) and magnification view and to compare endoscopic scores with Operative link for gastritis assessment (OLGA) and Operative link for gastric intestinal metaplasia assessment (OLGIM).

**Methods**: Total 28 patients underwent diagnostic esophagogastroduodenoscopy were enrolled and endoscopic scoring using NBI and magnification view were performed. Four areas (the lesser and greater curvatures of the antrum and the lesser and greater curvature side of the body) were observed and biopsies were taken. Degree of atrophy was scored from 0 to 2 according to Kimura-Takemoto classification (0: C0-2, 1: C3-O1, 2: O2-3). Degree of metaplasia was scored from 0 to 3 (0: no metaplasia, 1: metaplasia at antrum, 2: metaplasia at body, +1: 1/2 > observed filed). Endoscopic scores were compared to OLGA and OLGIM staging

**Results**: Correlation coefficients for atrophy between endoscopic and histologic scores 0.85 (95% CI: 0.70-0.93, $P < 0.001$) and those for metaplasia was 0.74 (95% CI: 0.85-0.87; $P < 0.001$). For atrophic gastritis, endoscopic score > 1 correlated OLGA Stage III and IV with a sensitivity, specificity, positive predictive value, and negative predictive value of 92%, 88%, 86% and 93%, respectively and for metaplasia, endoscopic score > 1 correlated high OLGIM Stage III and IV with those values of 78%, 100%, 100% and 73%, respectively.

**Conclusions**: Endoscopic scoring for gastric atrophy and intestinal metaplasia using NBI-magnification view seems to correlate well with histologic staging.

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## P2.03 | *Helicobacter pylori* induces alterations in liver cell signaling

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*Helicobacter pylori (HP)* is a human pathogen that causes chronic gastritis in about half of the world′s population. *HP* is usually acquired during early childhood and our immune system is not able to clear the infection. It has been long recognized that *HP* infection aggravates liver diseases and is a risk factor for the progression of liver cirrhosis and hepatocellular carcinoma (HCC). Additionally, co-infection with hepatitis C virus seems to enhance the severity of liver pathology. However, the mechanisms by which *HP* causes liver damage and promotes carcinogenesis remain largely unknown. We have shown that *HP* induces the rearrangement of actin cytoskeleton in infected primary hepatocytes or in hepatoma Huh7 cell line. Our current studies aim to determine the impact of *HP* infection on hepatocyte behavior and correlate the different *HP* strains with the alterations in cell signaling. Our work has shown that *HP* strains with different pathogenic outcomes alter the signaling of hepatocytes differently. *HP* oncoprotein CagA is phosphorylated in Huh7 cells and induces the activation of cellular ABL and ERK1/2 kinases. In addition, phosphorylated CagA results in the increase in CD44 levels. We have also investigated the inflammatory response of hepatocytes upon *HP* infection showing the NFkB activation and production of proinflammatory cytokines IL8, IL6 and TNFα. TNFα as well as certain *HP* strains alter liver cell migration in wound healing assay. Revealing the alterations in cell signaling and hepatocyte behavior upon infection will give insight into *HP*-induced liver pathogenesis.

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## P2.04 | Effect of *Helicobacter pylori* eradication on the lipid metabolic parameters

**P. YeWan**; J. Oh; T. Kim; H. Lee; Y. Min; B. Min; J. Lee; P. Rhee; J. Kim

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**Background**: There is a controversy as to whether *Helicobacter pylori* eradication can improve lipid metabolism. The aim of this study is to identify the effect of *H. pylori* eradication on lipid metabolism parameters.

**Method**: Among 1925 *H. pylori* infected patients who received eradication were included. The patients were divided into eradication succeeded and failed group, which was examined with $C^{14}$ breathing test or pathology. Propensity score matched analysis with age, sex, smoking/alcohol status, BMI was used to compare the difference in lipid metabolism indicators before and after eradication.

**Result**: Of the whole cohort, eradication of 1474 (76.6%) were succeeded. 303 patients were matched from each group. The differences of LDL-C, HDL-C, triglyceride, cholesterol of eradication succeeded vs failed group were −5.35 vs −2.56 ($P = 0.099$), 2.18 vs 1.43 (0.364), 3.20 vs 9.96 (0.463), −4.86 vs −2.52 (0.073), respectively.

**Conclusion**: Although the data analyzed didn't reach statistical significance, there was a tendency towards for lipid profiles to be improved after successful *H. pylori* eradication. Further studies are needed to confirm the effect of eradication on lipid metabolism.

**TABLE 1.** Characteristics of the study participants

| | All (n = 1925) |
|---|---|
| Age (years) | 53.2 ± 9.4 |
| Male (%) | 63.4 |
| BMI (kg/m$^2$) | 23.8 ± 2.9 |
| Waist circumference (cm) | 84.1 ± 8.9 |
| Current smoker (%) | 27.1 |
| Heavy alcohol intake (%) | 6.9 |
| LDL-C (mg/dL) | 118.8 ± 29.8 |
| HDL-C (mg/dL) | 55.5 ± 15.2 |
| Triglycerides (mg/dL) | 124.8 ± 92.5 |
| Total cholesterol (mg/dL) | 194.9 ± 33.7 |
| AST (U/L) | 24.5 ± 11.8 |
| ALT (U/L) | 25 ± 17.8 |
| FBG (mg/dL) | 98.3 ± 23.4 |
| Hypertension (%) | 19 |
| Diabetes mellitus (%) | 7.9 |

**TABLE 2.** Improvement of lipid metabolism parameters between the group with ***H. pylori*** eradicated and the group with ***H. pylori*** non-eradicated

| | *H. pylori* eradicated | *H. pylori* non-eradicated | *P*-value |
|---|---|---|---|
| LDL-C (mg/dl) | −5.35 ± 31.60 | −2.56 ± 31.95 | 0.0986 |
| HDL-C (mg/dl) | 2.18 ± 8.48 | 1.43 ± 9.80 | 0.3642 |
| Triglyceride (mg/dl) | 3.20 ± 92.04 | 9.96 ± 69.98 | 0.4915 |
| Cholesterol (mg/dl) | −4.86 ± 30.83 | −2.52 ± 32.49 | 0.073 |
| FBG (mg/dl) | 2.02 ± 22.14 | 3.92 ± 21.11 | 0.4923 |
| Albumin (g/dl) | 0.06 ± 0.27 | 0.08 ± 0.29 | 0.8549 |
| Platelet count (x $10^3$/μl) | −2.74 ± 28.20 | −2.52 ± 32.83 | 0.7686 |
| AST (U/L) | 0.48 ± 10.11 | 0.79 ± 12.06 | 0.9119 |
| ALT (U/L) | 1.19 ± 14.77 | 0.71 ± 15.39 | 0.5242 |
| Uric acid (mg/dl) | −0.03 ± 0.73 | 0.04 ± 0.84 | 0.3111 |
| CRP (mg/dl) | 0.02 ± 0.29 | −0.03 ± 0.33 | 0.3739 |
| Insulin (μIU/mL) | 0.31 ± 4.03 | 0.33 ± 3.79 | 0.7529 |
| Hemoglobin A1c (%) | 0.02 ± 0.56 | 0.02 ± 0.34 | 0.9464 |
| Abdominal girth (cm) | 0.67 ± 4.14 | 0.80 ± 4.07 | 0.7639 |
| Body fat (%) | 0.31 ± 2.76 | 0.32 ± 3.01 | 0.9249 |

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## P2.05 | *Helicobacter pylori* infection is inversely associated with self-reported cardiovascular disease in the GISTAR study population in Latvia

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**Introduction**: Higher prevalence of *Helicobacter pylori* (HP) has been reported in individuals with cardiovascular disease (CVD).

**Aim**: Evaluate the association of HP, CVD and its risk factors in Latvia.

**Methods**: 1855 participants aged 40-64 years that completed a questionnaire and were tested for HP IgG antibodies (Eiken Chemical, Japan) within the "*Helicobacter pylori* eradication and pepsinogen testing for prevention of gastric cancer mortality (GISTAR) study" in Latvia were included. Gender, age, education, income and cardiovascular risk factors - decreased vegetable/fruit (≤400 g daily), increased salt intake (adding extra to food), <150 minutes moderate exercise weekly, smoking, ethanol (g/week), diabetes mellitus, blood pressure and BMI were compared for participants positive (HP+) and negative (HP-) for HP, and with and without self-reported CVD. A multiple logistic regression model was built for CVD and HP+, including the factors above, additionally adjusting for history of peptic ulcer (associated with HP+ previously).

**Results**: HP+ was found in 1044 (56.3%) participants. CVD was reported by 528 (28.5%), of which myocardial infarction by 4.9% and stroke 4.7%. CVD was reported by 274 (26.2%) of those HP+ and 254 (30.2%) HP- ($P$ = 0.06). In multivariate analysis the association between self-reported CVD and HP strengthened (OR 0.73; 95% CI 0.57, 0.94; $P$ = 0.02) in comparison to univariate analysis (OR 0.82; 95% CI 0.67, 1.01; $P$ = 0.06).

**Conclusion**: We found HP to be inversely associated with self-reported CVD in contrast to most other studies showing either a positive or no association between HP and CVD.

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## P2.06 | Small intestinal bacterial overgrowth as predictor of *Helicobacter pylori* eradication inefficacy in diabetes mellitus patients

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**Background**: *Helicobacter pylori* (HP) eradication and antibiotic resistance are two major issues of modern gastroenterology. The results of many current studies indicate that the rates of successful HP eradication among patients with type 1 and 2 diabetes mellitus (DM) are lower than in nondiabetic subjects, but the causes for this are still unclear. Aim: To determine the role of small intestinal bacterial overgrowth (SIBO) in the efficacy of HP eradication among patients with type 2 DM.

**Methods**: 63 patients with type 2 DM and HP-associated chronic gastritis (30 men and 33 women, mean age 54.3 ± 11.2 years) underwent lactulose hydrogen breath test to detect SIBO. All the patients were prescribed standard 10-day triple therapy (Amoxicillin 1000 mg, Clarithromycin 500 mg, Pantoprazole 40 mg, bid). Eradication of HP was assessed by HP stool antigen test on the 28th day of the treatment.

**Results**: 35/63 (55.6%) patients with type 2 DM and HP-associated chronic gastritis were initially diagnosed with SIBO. Eradication of HP was achieved in 38/63 (60.3%) cases, 15/38 (39.5%) had concomitant SIBO. HP eradication therapy failed among 25/63 patients (39.7%), 20/25 (80.0%) subjects were diagnosed with SIBO. Thus, SIBO was associated with negative results of HP eradication therapy (RR: 3.2; 95% CI: 1.375-7.447; $P$ < 0.05).

**Conclusion**: These results suggest that SIBO may be considered as negative prognostic factor for successful HP eradication in patients with type 2 DM. Further large studies are needed.

I. Skrypnyk: None. T. Radionova: None.

## P2.07 | Is *H. pylori* infection of relevance in influencing GERD presentation? A comparison between typical and atypical GERD manifestations

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**Background and aim**: GERD is characterized by presence of typical and/or atypical symptoms. Diagnosis of GERD is made with EGD or gold standard Ph-metry/Ph-impedence. The role of H.p. in GERD is debated in Literature, but it's claimed that its presence is irrelevant in promoting GERD. The aim of this study was to investigate the role of H.p. in GERD, focusing on the association with typical and atypical symptoms.

**Materials and Methods**: Two groups of consecutive GERD patients were analyzed. Group A (216 pts, 118 F, mean age 48 years, range 26-89), showing typical symptoms and Group B (187 pts, 94 F, mean age 52 years, range 31-89), showing atypical symptoms, like ENT manifestations, non-cardiac chest pain, ecc. Diagnosis of GERD was made detecting esophagitis at EGD and/or positivity of pH-metry/pH-impedence off therapy. Patients were tested for H.p. with histology, UBT and serology, off therapy.

**Results**: H.p. was present in 84 /216 pts of group A (38.8%) and in 63/187 of group B (36.6%), without statistical difference between the two groups. Between patients with different symptoms presentation in group B (ENT vs chest pain), no difference was found as well as in group A between subjects showing heartburn vs regurgitation. No difference in rate of H.p. was found between sexes or grade of esophagitis (L.A. classification).

**Conclusions**: This study confirms the inconsistent role of H.p. in GERD, being no more than 30% of patients H.p. +. We demonstrated no difference of H.p. prevalence in GERD patients with typical and atypical symptoms.

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## P2.08 | Association between *Helicobacter pylori* infection with inflammatory and lipid metabolic profiles

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**Background**: Previous studies showed that *Helicobacter pylori* (*H. pylori*) infection is significantly related with altered metabolic parameters. We aimed to demonstrate the significant metabolic and inflammatory profiles associated with lower eradication rate and modification of such parameters after eradication.

**Methods**: We retrospectively analyzed various metabolic and inflammatory profiles such as hypertension, body weight, body mass index, waist circumference, HbA1c, fasting glucose, lipid profile and erythrocyte sedimentation rate (ESR) among subjects who received health check-up including surveillance esophagogastroduodenoscopy from 2013 to 2017 and were confirmed to have *H. pylori* infection.

**Result**: A total of 399 subjects were confirmed to be infected with *H. pylori* and received eradication therapy. Mean age was 49.7 ± 9.4 years and male was 72.2% (288/399). Eradication success rate was 84.9% (337/397) in 1st eradication regimen, 75.5% (40/53) in 2nd regimen and 94.5% (377/399) finally. Among inflammatory and metabolic profiles, ESR was significantly increased in subjects who finally failed eradication (15.7 ± 8.5 vs 11.8 ± 13.6 mm/hr, $P = 0.002$), and multivariate analysis showed that ESR ≥ 15 mm/hr was the only significant risk factor for lower eradication success rate (odds ratio; 0.22, 95% confidence interval; 0.09-0.54, $P = 0.001$). When comparing inflammatory and metabolic profiles before and after eradication therapy, serum low-density lipoprotein-C (LDL-C) was significantly reduced after eradication therapy among subjects who finally succeeded eradication (38.7 ± 2.8 vs 35.4 ± 2.6, $P = 0.02$), however, no parameters were significant changed among subjects who failed eradication.

**Conclusion**: *H. pylori* infection might be closely associated with hyperlipidemia and chronic inflammatory condition, which would be modified by successful eradication.

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## P2.09 | *Helicobacter pylori* and atopy markers: is there a relationship?

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The aim of study assess the prevalence infection and effects of infectious load of pathogen on atopic status in patients with AD.

The seroimmunological monitoring of HP was performed in patients with AD over a 10 year period (N = 2534). The study patients with a clinical diagnosis of AD to clinical and laboratory examination. The levels of IgG antibodies to the CagA HP antigen ("Helico-CagA-Ig G") with the calculation of the positivity coefficient (CP), which reflects level of infectious load. Study atopic status included level general and allergen-specific Ig E (acIgE Alkor-Bio, Immunocap). According to age factor 3 groups were formed: the first group included the children 2-5 years, the second group included the children 6-10 years, third group consisted of children over 10 years and adults. Determination of cIgE was carried out to the most common allergens: in 1 group - food, 2 group - food and inhalation, 3 group -inhalation.

**Results**: Seropositivity to CagA antigen was 18.5%. Direct correlations between CP and total Ig E in groups 1, 2, 3 and cIgE were recorded. In group 1, between CP and IgE to cow milk, egg white, wheat flour, soybeans, in groups 2 and 3 between CP and cIgE to dermatophagoides pteronyssinus, mixed fungi. Using methods of mathematical modeling, it is shown that effect on the parameters atopic status is different during age periods. Essential for assessing effect of HP on parameters atopic status are phenomena of non-specific and specific potentiation of sensitization shown in our study.

E.V. Agafonova: None. G.S. Isaeva: None. R.A. Isaeva: None.

## POSTER ROUND 2.2 GASTRIC MICROBIOTA

### P2.10 | Prevalence of *Helicobacter pylori* infection in patients with chronic hepatitis C virus infection in a northeastern Romanian center

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**Background**: *Helicobacter pylori*(*H. pylori*) infection is one of the most widespread infections in the world(ranging from 30 to 80% of the world's population), with the incidence depending on the socio-economic status. The prevalence of hepatitis C virus(HCV) infection worldwide is also influenced by the level of the socio-economic development access to health services. Worldwide, there are overlapping of the two infections in the same geographical areas.

**Aim**: To evaluate the prevalence of *H. pylori* infection in patients diagnosed with chronic HCV infection &lt to identify the common risk factors &gt the acquisition of the two infections.

**Material & method**: The study includes 107 patients admitted to Bacau County Emergency Hospital between November 1st 2018-April 1st 2019, diagnosed with chronic HCV infection confirmed by the detection of anti-HCV antibodies using ELISA. All patients were tested &gt anti-*H. pylori* antibodies by serological method. The data were statistically analyzed based on demographic &lt provenience criteria.

**Results**: From the total number of 107 patients included in the study, diagnosed with chronic HCV infection, 66 (61.68%) patients were diagnosed with *H. pylori* infection, predominantly women 47 (69.11%), from rural area in 36 (52.94%) cases, mean age 69 ± 9.8 years.

**Conclusions**: Although there are different transmission pathways, there is an increased incidence of *H. pylori* infection in patients diagnosed with chronic HCV infection. The level of socio-economic development &lt the access to medical services could be an explanation. Additional studies are needed to evaluate the relationship between *H. pylori* infection &lt chronic HCV infection.

E.V. Popovici: None.

### P2.11 | *Helicobacter pylori* and CagA *Helicobacter pylori* strain in children with gastroesophageal reflux disease (GERD)

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**Aim**: To study the association of *H. pylori* and CagA *H. pylori* strain with GERD in the children of Siberia (Russia).

**Materials and Methods**: We picked up by random 452 schoolchildren (in the ages from 7 to 17 years) in Siberia, Russia. In them GERD was diagnosed in accordance with Montreal Consensus (Vakil N. et al., 2006). All the children had been performed gastroscopy with biopsy and blood serum sampling. *H. pylori* was identified by morphological method after Gimza coloring. Immune enzyme method was used for identifying CagA *H. pylori* in blood.

**Results**: As a whole in children population *H. pylori* prevalence didn't correlate to GERD (58.9% with GERD and 60.2% without GERD; $P = 0.8175$). In the age group from 7 to 11 years *H. pylori* among GERD subjects amounted to 50.0%, without GERD – 51.4% ($P = 0.8175$); in the ages from 12 to 17 years 60.5% and 64.1% accordingly ($P = 0.5665$). CagA *H. pylori* in schoolchildren had been diagnosed in 51.1% in GERD patients and in 47.8% without GERD ($P = 0.6821$). In the age group from 7 to 11 years the frequency of the strain was 28.6% with GERD and 46.1% without the pathology ($P = 0.3732$). In the ages from 12 to 17 years the presence of CagA *H. pylori* was determined in 55.3% and 48.6% correspondingly ($P = 0.4669$).

**Conclusion**: *H. pylori* and its strain CagA association with GERD in the children of Siberia hadn't been revealed in the children of Siberia, including different age cohorts.

T.V. Polivanova: None. V.V. Tsukanov: None. V.A. Vshivkov: None.

## P2.12 | Differences in gastrointestinal microbiota in INS-GAS mice housed at different facilities affect *H. pylori* induced gastritis

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Gastrointestinal microbiota play an important role in *H. pylori* induced gastritis and the development of gastric adenocarcinoma (GC). Transgenic insulin-gastrin (INS-GAS) mice develop spontaneous atrophic gastritis and gastrointestinal intraepithelial neoplasia (GIN) and have been used to investigate the mechanism *H. pylori* induced GC. Germfree INS-GAS mice have a delayed development of *Hp*-promoted GC compared to specific pathogen-free (SPF) mice. Colonization with three bacterial species enhanced the development of high grade GIN compared with *H. pylori* mono-infected germfree mice. We compared the fecal microbiota of MIT maintained INS-GAS mice to INS-GAS mice originally housed at Norwegian University of Science and Technology (NTNU) and shipped to MIT. Upon arrival, mice from NTNU were housed in SCID conditions in a biocube at MIT. Significant differences in alpha and beta microbiome diversities were observed between the two colonies. Forty mice from each colony were infected with *H. pylori* PMSS1. *H. pylori* colonization levels, gastric pathological scores, stomach cytokine mRNA expression and fecal microbiota compositions were evaluated at 8 and 16 weeks post infection (wpi). MIT mice at 16 wpi had significantly higher gastric pathological scores and higher *H. pylori* colonization than NTNU mice. Higher gastric expression levels of *Il1*-β, *Ifn*-γ, *Tnf*-α and *iNos* were noted in *H. pylori* infected MIT mice compared to NTNU mice. *H. pylori* infection significantly increased levels of *Lactobacillaceae* in the feces of MIT mice compared to NTNU mice. Our results emphasize that differences in GI microbiota in the same strain of mouse can cause different responses to *H. pylori* leading to different disease outcomes.

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## P2.13 | Gastric colonization with non-*H. pylori* urease positive bacteria and their effects on *H. pylori* pathogenesis

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Human stomachs are often colonized by non-*H. pylori* bacteria. Changes in composition or structure of bacterial communities in the stomach may contribute to gastric pathology. Thirty-seven *H. pylori* positive or *H. pylori* negative patients from the low-gastric-cancer-risk (LGCR) region of Tumaco, and the high-gastric-cancer-risk (HGCR) region of Pasto, Colombia were recruited for gastric endoscopy and gastric microbiome analysis by bacterial culture and culture-independent 16S rDNA sequencing. The gastric microbiota composition was variable between the regions and *H. pylori* status. Sixty-six distinct species of 26 genera were isolated by culture, the top five most commonly isolated non- *H. pylori* genera were *Bacillus*, *Streptococcus*, *Staphylococcus*, *Veilonella*, and *Actinomyces*. Urease positive *Staphylococcus epidermidis and Streptococcus salivarius* were frequently isolated from biopsies. We asked whether coinfection of *S.salivarius* and *S.epidermidis* with *H. pylori*, had a demonstrable effect on *H. pylori*-induced gastritis in germfree INS-GAS mouse model. The germfree INS-GAS mice co-infected with *H. pylori* and *S.salivarius* had statistically higher gastric pathological scores when compared with *H. pylori* only or *H. pylori* with *S. epidermidis* infected mice at 5 months post infection. *S.epidermidis* co-infection with *H. pylori* did not change stomach pathology significantly; however pro-inflammatory cytokines Il1-β, Il17-a and Il22 levels were significantly lower than these cytokines in the *H. pylori* only group. Using *in vitro* assays, *S.epidermidis* inhibited *H pylori* growth, reduced the numbers of *H. pylori* adhered to AGS cells. *S.salivarius* increased *H. pylori* induced IL8 production and upregulated chemokine gene expressions in AGS cells. This study reinforces the argument that non-*H pylori* bacteria can play a role in the severity of *H. pylori* induced gastric cancer.

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## P2.14 | The network construction and module organization of gastric microbiome and its association with gastric carcinogenesis

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**Introduction**: Gastric microbiome dysbiosis has been known to be associated with gastric carcinogenesis. However, modules of interacting bacteria (rather than individual bacteria) associated with gastric carcinogenesis have yet to be clarified.

**Methods**: Gastric mucosal tissues were obtained from the Hanyang University Gastric Microbiome Cohort. Gastric mucosal microbiome was analyzed by 16S rRNA gene sequencing. Construction of microbiome network and detection of a microbial module were performed using weighted correlation network analysis. Then, relationships between gastric carcinogenesis and microbial modules were evaluated using eigenvalue networks.

**Results**: Gastric microbiome data from 83 participants were evaluated. We identified 18 microbial modules through the weighted correlation network analysis. Among them, two modules, named pink and brown modules, were shown to be associated with advanced stage of gastric carcinogenesis such as *Helicobacter pylori* non-infected intestinal (correlation coefficient between module eigenvalue vs ABCD group: pink module, 0.31 [$P$ = 0.004], brown module, 0.26 [$P$ = 0.02]). The pink and brown modules consist of 22 and 32 different bacterial taxa at the family level, respectively. Those modules included various T4SS bacteria, such as Neisseriaceae, Pasteurellaceae, and Acidobacteriaceae in the pink module and Bartonellaceae, Pseudomonadaceae, and Xanthomonadaceae in the brown module. In the visualization of full weighted networks in the pink and brown modules, high correlation strengths were observed.

**Conclusion**: The highly correlated gastric microbial modules can be classified by stage of gastric carcinogenesis. Microbial modules may provide an integrative view of microbial ecology relevant to a precancerous lesion in the stomach.

C. Park: None.

## P2.15 | The dysbiosis of mucosa-associated gastric microbiota during aging

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**Background**: Although the incidence of gastric cancer and its precursor lesions increases dramatically with advancing age, the precise role of aging in that increase remains unclear. This study aimed to investigate the alterations of gastric microbiota other than host factor during aging.

**Methods**: A total of 30 asymptomatic individuals were enrolled in this study, including 10 young and 20 elderly adults. Ten young and seven elderly subjects were diagnosed as *Helicobacter pylori* (*H. pylori*) positive and only the young adults received eradication therapy. The gastric mucosa samples were collected at baseline and after eradication. The 16S rRNA gene sequencing was applied to analyze the structure of gastric microbiota.

**Results**: A sharp reduction of within-individual microbial diversity was noted in elderly subjects compared to young subjects. The composition of gastric microbiota was significantly different between young and old adults, which was independent of *H. pylori* infection. The relative abundance of *Pseudomonas* and *Enterococcus* was significantly increased in old compared with young individuals, while some beneficial bacteria such as *Bifidobacterium*, *Faecalibacterium* and *Blautia* were decreased. The capacity for the inferred pathway, Lipopolysaccharide biosynthesis proteins, was significantly increased in old compared to young subjects. Notably, the impact of *H. pylori* on the gastric microbiota in young volunteers was larger than those observed in old subjects.

**Conclusions**: The structure of gastric microbiota changed with the increase of age. The dysbiosis of gastric microbiota in old population may be associated with the development of pre-cancerous lesions and even gastric cancer.

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## P2.16 | Gastric yeast can harbor a collection of endosymbiotic bacteria

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**Background**: Coexistence of bacteria and fungi in a wide range of habitats refers to the likelihood of existence of bacteria inside fungi such as yeast. Even a collection of intracellular bacteria might coexist in a fungal cell. The most abundant bacteria in nature, actinomycetes and cyanobacteria could be candidates for fungal endobacteria. Interestingly, *Helicobacter pylori* which coexist with yeast in human stomach could be another candidate. In this study, the likelihood of intracellular existence of three mentioned bacteria in yeast was assessed using PCR.

**Methods**: Fifteen gastric yeasts were identified using Chromagar. Pure cultures of yeasts were subcultured on yeast glucose chloramphenicol agar more than 10 times. Yeasts total DNA was extracted and examined for the presence of *H. pylori*-, actinomycetes- and cyanobacteria- specific *16S rDNA*.

**Results**: Two yeasts were identified as *Candida albicans*, one *C. tropicalis* and the rest *Candida* spp. Out of fifteen yeasts, 10 (66.6%) carried *H. pylori*, 11 (73.3%) actinomycetes and 13 (86.6%) cyanobacteria. Six yeasts (40%) carried all three *H. pylori*, actinomycetes and cyanobacteria.

**Conclusion**: Results of this study showed the occurrence of multiple endosymbiotic bacteria inside yeasts. Details of bacterial endosymbiosis in yeast remain to be elucidated. However, yeast has been suggested as a nutritive and protective niche for bacteria. Beneficial role of bacteria for yeast could be creating vacuole by *H. pylori* VacA, protecting against competitors by antibiotic producing actinomycetes and using light energy by photosynthetic cyanobacteria. Accordingly, eukaryotes such as yeast exploit one or more endobacteria for a diverse range of activities.

F. Siavoshi: None. S. Heydari: None. H. Ebrahimi: None.

## P2.17 | Does the next generation sequencing (NGS) strategy affect the diversity measures in gastric microbiota?

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**Introduction**: NGS techniques have evolved quickly in the last few years. Results comparison is not always easy as each instrument has its own technology

Aim: to compare the alpha and beta-diversity measures after parallel gastric microbiome study using two different NGS strategies in *H. pylori* infected and non-infected paediatric patients.

**Materials and Methods**: Gastric biopsies from 21 paediatric patients were studied: ten HP-positive (positive HP-culture) and eleven HP-negative (negative by culture, rapid urease test and histology). 16SrRNA-based microbiome study was performed using 454 (Roche) and MiSeq (Illumina) using the same nucleic acid extract. Alpha-diversity (Shannon index and Student T statistical test) and beta-diversity measures (weightened and unweightened Unifrac, PCoA and ANOSIM statistical test) were performed using QIIME and SPSS.

**Results**: Shannon index was: in HP-negative, 4.45 (±0.72) by MiSeq and 2.27 (±1.57) by 454; in HP-positive, 1.54 (±1.49) by MiSeq and 2.03 (±1.92) by 454.

In beta-diversity comparison, statistically significant results were obtained in both NGS strategies for HP-positive vs negative culture (unweighted and weighted) but only for MiSeq (uweighted and weighted) in histology findings.

**Conclusions**: Results obtained using 454 and MiSeq are no completely equivalent.

Differences are more remarkable in alpha-diversity that in beta-diversity measures.

Differences can be due to pre-sequencing treatments (i.e. PCR strategy), sequences length (shorter in MiSeq), the fact that MiSeq is paired-ends and 454 is single-ends or the amplified region of 16SrARN (V3-V4 in MiSeq and V1-V4 in 454).

A common and standardised sequencing algorithm is needed to be able to compare results between studies.

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## P2.18 | Helicobacter and gastric microbiota in relation to carcinogenesis

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Gastric cancer is one of the prevalent cancers in the world, for which microbial effects are well explained in cancer development: *Helicobacter pylori* infection triggers the carcinogenesis process. Recent reports, however, suggest the possibility that *H. pylori* is not the sole microbial source causing the gastric cancer. We hypothesized that there are some bacteria which act as inhibitors or accelerators of carcinogenesis. Therefore, the aim of this study is to characterize microbiota structures of the stomach in accordance with disease states. 16S rRNA sequence analysis was performed to the collected biopsy samples from several disease states including atrophic gastritis, intestinal metaplasia and gastric cancer as well as from normal states including superficial chronic gastritis. The gastric microbial structure shows a large variation that depends on individuals, however mostly constitutes of five phyla: *Actinobacteria*, *Bacteroidetes*, *Firmicutes*, *Fusobacteria* and *Proteobacteria*. Abundance of *H. pylori* is a factor that affects significantly to the gastric microbial structure. In ß-diversity analysis, samples are clustered according to its *H. pylori* abundance. However, the abundance of *H. pylori* is not consistent with disease states. We found gastric microbial structures can be stratified into several groups that are associated with normal or disease states. In this study, we characterized group-specific taxa and analyzed correlation between taxa and disease. This study allows us to understand the gastric microbiota structure and provide us a possibility to develop microbiota-based pharmabiotics.

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## P2.19 | Identification of culturable bacteria isolated from gastric biopsies of dyspeptic patients

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**Introduction**: It is now quite established that the human stomach supports a bacterial community with a considerable diversity. It appears that in addition to *Helicobacter pylori* as a unique colonizer of gastric niche, other bacteria can reside in this hostile acidic habitat.

The aim of this study was detection of culturable bacteria in patients with dyspepsia.

**Method**: Gastric biopsies taken from 50 dyspeptic patients were cultured on selective (with antibiotics) and nonselective Brucella blood agar (BBA). Plates were incubated at 37°C under microaerophilic conditions and bacterial growth examined after 5-10 days. Bacterial isolates were identified according to biochemical characteristics.

**Results**: Out of 50 gastric biopsies 31 did not show bacterial growth. Out of 19 remaining biopsies, 7 were positive for *H. pylori* only without any other bacteria, 11 showed growths of 12 bacteria and one contained *H. pylori* as well as one bacterium. *H. pylori* showed spiral morphology and positive activities of urease, catalase and oxidase. The 12 bacteria included *Corynebacteria (C. pygenes 3x*, *C. heamolyticum 2x and Corynebacterium* spp.*)*, *Pasteurella (P. ureae*, *P. maltocida 2x)*, *Acinetobacter calcoaceticus*, *Branhamella catarrhalis*, *Plesiomonas shigelloides*. The bacterium isolated along with *H. pylori* was identified as *Clostridium ramosum*.

**Conclusion**: Results of this study showed that gastric biopsies with *H. pylori* were devoid of bacterial contaminations. It appears that occurrence of *H. pylori* might protect gastric epithelium from colonization by other bacteria. Bacterial isolations from gastric biopsies indicate existence of a diverse range of bacteria that might play role in development of gastric diseases.

F. Siavoshi: None. G. Poostizadeh: None. S. Kadkhodaei: None. H. Ebrahimi: None. A. Sajadi: None.

## POSTER ROUND 3.1 GUT MICROBIOTA IN HEALTH AND DISEASE

### P3.01 | *Helicobacter pylori* infection shapes intestinal immune responses and microbiota signatures

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*Helicobacter pylori* infection is one of the most prevalent infections worldwide and although colonizing the stomach, chronic infection leads to systemic consequences. Upon entering the host, *H. pylori* leads to a strong T-cell response in the stomach, whereas intestinal lymphatic organs most probably are the early priming sites of the infection. Furthermore, it not only alters the composition of the gastric but also induces changes in the intestinal microbiota. Considering the close proximity and natural route of digestion, we hypothesize that *H. pylori* infection also affects the digestive tract by altering intestinal and colonic immune homeostasis and shaping microbiome signatures.

We conducted a comprehensive analysis of alterations in the intestinal and colonic immune response as well as the gut microbiota upon *H. pylori* infection by comparing infected with non-infected C57BL/6 mice using immunohistochemistry, qPCR, flow cytometry and 16S RNA Sequencing.

*H. pylori* infection leads to a decreased alpha diversity in stomach, intestine, caecum, colon and stool and is negatively associated with the relative abundance of *Clostridium XIVa* and positively with *Akkermansia spp*. Furthermore, we observed an increased recruitment of T-cells into the intestinal and colonic epithelia upon infection and a *H. pylori* specific CD4+ IFNγ and IL-17 T cell response in the lamina propria of the intestine.

Overall, this study shows that *H. pylori* infection affects intestinal homeostasis by altering gut microbiota and immune responses.

A. Ralser: None. N. Cullin: None. R. Mejías-Luque: None. M. Gerhard: None.

### P3.02 | Alteration in the abundance of Akkermansia muciniphila is associated to gastrointestinal and extra-intestinal diseases: Towards the identification of specific microbial markers of dysbiosis

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Gut microbiota exerts a crucial role in several GI and extra-intestinal (EI) diseases. The aim was to investigate potential common disease microbial biomarker(s) of dysbiosis between different GI and EI diseases. 84 patients (D) with a diagnosis of IBD, IBS, celiac disease, anxiety disorder, eating disorders, autoimmune thyroiditis, autism spectrum disorders, PANDAS and diabetes were included in the study and fecal samples were collected. 85 controls (C) matched for age and sex were also enrolled. Genomic DNA was extracted and V3-V4 regions of the 16S rRNA gene were sequenced by MiSeq Illumina platform. At unsupervised analysis, hc evaluation identified a clear clusterization between D and C. β-diversity assessment evidenced a specific phylogenetic diversity between the two groups. Relative abundance analysis found Verrucomicrobia and Actinobacteria significantly decreased in D vs C. *Akkermansia muciniphila* resulted the most robustly reduced genera in D vs C. Random Forest evaluation reinforced these observations. A reduction of *Akkermansia muciniphila*, *Bacteroides* and *Bacteroides Ovatus* represented the most relevant discriminant factor between the two groups. Through machine learning techniques, *Akkermansia muciniphila* was identified as a crucial node to differentiate D from C. At supervised computational analysis *Akkermansia muciniphila* levels resulted able to discriminate the two groups and ROC curve application on the glm model defined the best discriminating threshold of 2.5%. *Akkermansia muciniphila* decline represents a definitive biomarker of dysbiosis shared by patients with different GI and EI and the most relevant

discriminating factor able to dissect the complex equilibrium between the health and disease status.

L. Lopetuso: None. A. Quagliariello: None. M. Schiavoni: None. V. Petito: None. G. Ianiro: None. F. Del Chierico: None. G. Cammarota: None. F. Scaldaferri: None. L. Putignani: None. A. Gasbarrini: None. A. Russo: None. S. Reddel: None.

## P3.03 | Microbiota-dependent toll-like receptor 4 signaling by endothelial cell affects platelet deposition in arterial thrombosis

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Introduction: The gut microbiota impacts host physiology and affects carotid artery thrombosis through Toll-like receptors (TLRs). Here, we studied the role of TLR4 on endothelial cells and platelets in a mouse model of arterial platelet deposition.

**Methods**: We applied intravital microscopy to investigate platelet deposition following carotid artery injury in WT, *Tlr4*-deficient (*Tlr4*$^{-/-}$) and endothelial-specific *Tlr4*$^{-/-}$ mice, which were also treated with antibiotics. Effects of platelet TLR4 were analysed by depleting platelets in WT mice and reconstitution with WT or *Tlr4*$^{-/-}$ platelets. As a control, TLR4 was inhibited in WT mice with CLI-095. Thrombin formation in platelet-rich plasma was measured by the calibrated automated thrombin generation (CAT) assay. Following inhibition of thrombin (Argatroban), platelet deposition to the injured carotid artery was analysed.

**Results**: *Tlr4*$^{-/-}$ mice showed a reduction of platelet deposition to the injury carotid artery. Involvement of TLR4 signaling was corroborated by inhibition of TLR4 in WT mice. CAT analyses showed that activation of platelet TLR4 signaling contributes to thrombin generation. Blocking of thrombin resulted in reduced platelet deposition in WT, but not in *Tlr4-/-* mice. *Tlr4* deficiency on platelets does not affect platelet binding, while *Tlr4* deficiency on endothelial cells restored the reduced platelet adhesion. Antibiotic treatment indicated that this effect is microbiota dependent.

**Conclusion**: Our results demonstrate a role for endothelial TLR4 signaling in tissue factor-triggered thrombin generation. In vivo, impaired TLR4 signaling in the endothelium resulted in reduced platelet deposition to the injured carotid artery, which was dependent on thrombin activity and the gut microbiota.

A. Grill: None. S. Jäckel: None. G. Pontarollo: None. C. Karwot: None. C. Reinhardt: None. C. Joseph: None. B. Rauch: None.

## P3.04 | Effects of proton pump inhibitors on the microbiome of the digestive tract - A systematic review

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Proton pump inhibitors (PPIs) are widely used to treat acid-related disorders of the upper gastrointestinal tract. Observational studies have raised concerns about possible adverse events, including enteric infections and gastric cancer, although the evidence for causality of these associations is limited. Recently, PPIs have been demonstrated to affect the composition of the intestinal microbiome. With increasing recognition of the gut microbiota in health and disease, PPI-induced dysbiosis is speculated to mediate associated adverse effects. We systematically reviewed the literature about the influence of PPIs on the intestinal microbiome in humans. A PubMed search yielded 197 records. 24 publications met the prespecified eligibility criteria - most importantly the use of culture-independent techniques and human study populations - and were included in the review. In most studies, PPIs do not affect established richness and diversity measures but cause distinct taxonomic alterations: In the esophagus, stomach and duodenum, PPIs promote overgrowth of orally derived bacteria, mostly of *Streptococcaceae*. In fecal samples, PPIs increase multiple taxa from the orders *Bacillales* (e.g., *Staphylococcaceae*), *Lactobacillales* (e.g., *Enterococcaceae*, *Lactobacillaceae*, *Streptococcaceae*) and *Actinomycetales* (e.g., *Actinomycetaceae*, *Micrococcaceae*), the families *Pasteurellaceae* and *Enterobacteriaceae* and the genus *Veillonella*. Taxa decreased by PPIs include the families *Bifidobacteriaceae*, *Ruminococcaceae* and *Lachnospiraceae* and the class *Mollicutes*. Collectively, these data support the hypothesis that PPI-induced hypochlorhydria allows upper gastrointestinal microbiota to colonize more distal parts of the gastrointestinal tract. Despite emerging evidence that PPIs alter the gut microbiome, a causal involvement of PPI-induced dysbiosis in health and disease is currently not substantiated by scientific evidence.

L. Macke: None. C. Schulz: None. J. Mayerle: None. P. Malfertheiner: None.

## P3.05 | *Campylobacter taeniopygiae* sp. nov., *Campylobacter aviculae* sp. nov., and *Campylobacter estrildiarum* sp. nov., novel species isolated from laboratory maintained Zebra Finches

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Zebra finches (*Taeniopygia guttata*) are commonly used laboratory animal species for modelling neurobiology and learning. Historically

bacterial isolates from feces of finches housed at MIT have been presumptively diagnosed as of *Campylobacter jejuni*, a microaerophilic bacteria commonly isolated from both domestic and wild birds. *C. jejuni* is a known zoonotic pathogen that causes gastroenteritis in humans worldwide. Human transmission is predominantly foodborne and associated with consumption of contaminated poultry; however, humans can also become infected from contact with *C. jejuni* infected reservoir hosts. Because *C. jejuni* infected finches pose a risk to research personnel, a study was undertaken to investigate the prevalence and taxonomic identification of *Campylobacter* spp. present in the finch colony. A total of 26 finch fecal samples collected in 2003, 2010, and 2017, had *Campylobacter* spp. isolated from all the samples. 16S rRNA sequencing of all isolates determined that they shared 99% identity with either *C. jejuni* or *C. lari*. Sixteen of the isolates were subjected to further biochemical characterization, *atp*A and *rpo*B gene sequence analysis. Based on these analyses, three clusters of *Campylobacter* species were identified. Whole genome sequences were obtained for one representative isolate from each cluster. Pan-genomic phylogenetic tree, average nucleotide identity, digital DNA-DNA hybridization, and orthologous gene analyses indicated that each isolate was its own novel species, distinct from *C. jejuni*, and other avian species. We have named these novel species *C. taeniopygiae*, *C. aviculae* and *C. estrildiarum*, and in each novel species have identified virulence genes suggesting their pathogenic and zoonotic potential.

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## P3.06 | Gut microbiota at school age: Influential factors and associations with cognitive development: Preliminary results

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**Background**: The understanding of determinants of the gut microbiota at school-age and the role of gut microbiota in children's health remains limited.

We assessed correlates the gut microbiota composition of healthy school-age children and examined associations of gut microbiota with children's cognitive development.

**Methods**: A study of 176 children 6-9 years old was undertaken in 3 neighboring Arab villages in Israel, representing low, intermediate and high socioeconomic status (SES) communities. Analysis of the gut microbiome was conducted using16S sequencing. Sociodemographic and health information was collected. Cognitive assessment yielding intelligence quotient (IQ) score was performed.

**Results**: Children from the low SES village had a distinct microbiome composition compared to children from the intermediate/high SES villages, who had similar microbiome (ANOSIM $R = 0.28$, $P = 0.001$). Alpha diversity (Shanon index) and the relative abundance of main genera differed significantly by village. The genus Bacteroides was less common in children from the low SES village vs those from the intermediate/high SES villages.

A negative correlation was found between the relative abundance of Prevotellaceae and IQ score (Spearman's rho −0.40, $P < 0.0001$ adjusted by false discovery rate method), while a positive correlation was found with Bacteroidaceae (Spearman's rho 0.44, adjusted $P < 0.0001$).

**Conclusions**: The gut microbiome of school age children differed by residential SES, within a well-defined geographic region and population. Bacteroidaceae, was related to better cognitive development, while Prevotellaceae was related to worse. The gut microbiota might reflect a certain lifestyle that affect children's development, or could be linked directly to cognitive development via gut-brain axis, or both.

K. Muhsen: None. L. Reshef: None. A. Ornoy: None. M. Maya: None. U. Gophna: None. D. Cohen: None.

## P3.07 | *Proteus mirabilis* urease: Unsuspected non-enzymatic properties that potentially contribute to pathogenesis

V. Broll[1]; F. C. Lopez[1]; A. H. S. Martinelli[1]; N. R. Moyetta[2]; N. R. Moyetta[2,3]; L. L. Fruttero[2,3]; M. V. C. Grahl[2]; A. F. Uberti[2]; D. R. Demartini[1]; R. Ligabue-Braun[1,4]; **C. R. Carlini**[2]

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Urinary infection by the gut bacteria *Proteus mirabilis* leads to kidney and bladder stones and incrustation of catheters due to ammonia generation catalyzed by its urease (PMU), a pivotal virulence factor of this uropathogen. In the last twenty years, ureases have been characterized as multifunctional proteins endowed with biology properties unrelated to their enzyme activity, that could potentially contribute to the pathogenesis of diseases caused by *P. mirabilis*. PMU is an enzyme composed of three subunits, PmUreα, PmUreβ and PmUreγ, in an $(\alpha\beta\gamma)_3$ organization. Here, we evaluated non-enzymatic properties of a recombinant enzymatically active PMU and of its separate subunits. Similar to plant ureases, PMU displayed antifungal activity and lethal effects in insects. Nanomolar concentrations of PMU promoted aggregation of human platelets, an effect previously correlated to pro-inflammatory properties of other ureases. Like jaburetox, a polypeptide derived from a plant urease, the PmUreβ subunit was toxic against yeasts and insects, and also aggregated platelets. PmUreα (containing the catalytic site) and PmUreγ were weakly or not active in the bioassays, hence PmUreβ carries most

of the non-enzymatic activities of PMU. Bioinformatics analyses revealed gene/segment duplication of PmUreβ spanning PmUreα as well as its homology to jaburetox, uncovering the evolutionary divergence among ureases. Our data indicate that *P. mirabilis* urease is a multifunctional protein displaying non-enzymatic biological properties that may contribute in unsuspected ways to the pathogenesis of urinary infection besides promoting urinary stone formation.

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## P3.08 | Microbiome alterations and the development of risk factors for irritable bowel syndrome in a cohort of German patients

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Irritable bowel syndrome (IBS) is one of the most common gastrointestinal disorders worldwide. Despite the prevalence and burden on quality of life, the pathogenesis of IBS is poorly understood, making diagnosis of IBS difficult. In fact, IBS has been linked to diet, psychiatric and sensory disorders, and potentially to alterations within the gastrointestinal microbiota. Understanding how these potential causes of IBS correlate with symptoms could lead to more effective diagnostics. We hypothesize that changes within the microbiome correspond to the development of IBS-like symptoms; therefore, we aim to characterize microbiome alterations via 16S *rRNA* sequencing in the hopes of identifying potential risk factors. In this pilot study, forty patients who initially visited a physician with complaints of prolonged abdominal pain were followed for six months. Patients completed regular questionnaires regarding their health and symptoms. Stool was collected at time of enrollment, three months, and six months for examination of the microbiome. Bacterial DNA was extracted from stool samples using the Stratec PSP Spin Stool DNA Plus Kit. Sequencing of indexed and pooled 16S amplicons was performed on an Illumina MiSeq and downstream bioinformatics analysis performed using taxonomic data generated from the Integrated Microbial Next Generation Sequencing Platform. We could identify distinct *alpha* diversity shifts over time in the patient cohort. Furthermore, as compared to a control cohort, patients showed significantly lower relative abundances of families Lachnospiraceae and Prevotellaceae, indicating that after further correlation to symptoms, microbiome analyses may have potential as a diagnostic tool for patients with IBS-like symptom development.

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## P3.09 | Effect of probiotics in children with infantile eczema

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**Objective**: Probiotics are used in the treatment of several conditions: functional abdominal pain, infantile colic, celiac disease, irritable bowel syndrome, lactose intolerance, food allergy, Hp infection, asthma, atopic dermatitis and infantile eczema. To determine whether oral administration of the probiotic Lactobacillus GG under randomized, double-blinded, placebo-controlled conditions would improve symptoms of infantile eczema in children.

**Patients and methods**: 41 children with infantile eczema were given Lactobacillus GG or placebo for 6 weeks and entered follow-up for 4 weeks. Children entered a randomized, double-blind, placebo-controlled trial.

**Results**: LGG, but not placebo, caused a significant reduction of both frequency ($P < .01$) and severity ($P < .01$) of eczema. These differences still were significant at the end of follow-up ($P < .02$ and $P < .001$, respectively).

**Conclusions**: Lactobacillus GG was superior to placebo in the treatment of eczema in children. The intestinal microbial flora may contribute to the pathogenesis of allergic diseases, LGG significantly reduces the frequency and severity of infantile eczema and maybe because improves the gut barrier function and reduce the inflammatory response.

T. Sabbi: None.

## P3.10 | Dysbiosis, gut microbiota modulation and intestinal permeability in recurrent cystitis patients and concomitant gastrointestinal pathologies

C. Graziani[1]; F. Scaldaferri[1]; C. Talocco[1]; J. Gervasoni[1]; S. Persichilli[1]; A. Primiano[1]; V. Petito[1]; A. Quagliariello[2]; F. Del Chierico[2]; L. Putignani[2]; L. Lopetuso[1]; A. Urbani[1]; **M. Napoli**[1]; A. Gasbarrini[1]

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Urinary tract infections (UTIs) affect over 50% of women, of which at least 20-30% develop a recurrence. Of these, up to 5% will experience chronic recurrent infections. Urinary infections seem to be caused mainly by agents deriving from the intestinal microbial flora, of which the major representative was E. coli. Intestinal contiguity contributes to the etiopathogenesis of recurrent cystitis. Intestinal

permeability is a clinical entity associated to intestinal and extra-intestinal diseases. It is an overall measure of intestinal homeostasis and gut barrier integrity. However a potential role of intestinal permeability and dysbiosis cannot be excluded. To study the variations of intestinal permeability and dysbiosis in patients, suffering from recurrent cystitis referred to gastroenterologist. Patients with recurrent cystitis showed significantly higher symptoms score of diarrhea, constipation, abdominal pain compared to controls and all showed an increase in intestinal permeability. Breath Test highlighted an increased prevalence of SIBO and alterations of oro-cecal transit in patients compared to controls. Microbiota characterization showed an incipient dysbiosis with a slight no significant reduction of α-diversity, of CHAO Index and Shannon Index compared to controls. However, a trend of reduced biodiversity was observed. Potential marker of dysbiosis in recurrent cystitis seem to belong above all to the phylum of the Firmicutes, such as Ruminococcus, Blautia, Veillonella, Streptococcus spp. Patients with recurrent cystitis seem to show high prevalence of disorders gastro-intestinal, increased permeability and dysbiosis with a prevalence of more than 20%.

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## P3.11 | Structural changes in gut microbiome of diabetic mice after Reboxetin treatment

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Antidepressants are widely used drugs in clinical settings. However there is very limited number of study on the effect of these drugs on gut microbiota. Herein, we evaluated the effect of reboxetin (RBX), which is a norepinephrine reuptake inhibitor on gut microbiota in both diabetic and nondiabetic mice. To the best of our knowledge, this is the first report on effect of reboxetin use on gut microbiota.

Diabetes is induced in mice by using streptozotocin (STZ). Reboxetin was introduced in two different doses during 14 days to diabetic mice (STZ/16 mg/kg RBX, n = 6; STZ/8 mg/kg RBX, n = 6; STZ alone, n = 6) and healthy controls (Control/16 mg/kg RBX, n = 2; Control/8 mg/kg RBX, n = 2; Control alone, n = 7). Stool samples were collected after the end of RBX treatment. Following DNA extraction, amplicon libraries were prepared for V4 region and sequenced with Illumina Miseq platform. QIIME was used for preprocessing and analyzing of the data.

There was no significant differences in none of the groups in terms of alpha diversity metrics. However, unweighted UniFrac analysis were significantly different ($P$ = 0.001). Different doses of RBX also have a distinct effect in terms of beta diversity. Both RBX treatment and diabetes status have significant effects on composition of the gut microbiota. Within diabetic mice groups, RBX treatment lead to significant increase on Prevotella, Flexispira, Oscillospira, Bacteroides groups according to LefSe analysis.

This experiments showed that RBX has a distinct effect on gut microbiota structure and composition in both diabetic mice and healthy mice.

S. Tekinkoca: None. C. Ozkul: None. H. Gencer: None.

## P3.12 | Norepinephrine modulates virulence of adherent-invasive *Escherichia coli* strains associated with Crohn's disease in children

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**Aim**: In the study, we investigated the effect of norepinephrine (NE) on the interaction of six adherent-invasive *E. coli* (AIEC) strains isolated from intestinal biopsy specimens of children with Crohn's disease, with differentiated Caco-2 cells.

**Methods**: The growth rates, an *in vitro* adherence and invasion assays, and survival in human macrophages of *E. coli* exposed to NE were investigated. We also determined the effect of NE on the expression of *ompA*, *fimA* and *fliC* genes in *E. coli* strains.

**Results**: We found that NE had no appreciable effect on the growth rates of AIEC but significantly increased their adherence and invasion into polarized Caco-2 cells. NE had a differential, strain-dependent effect on the expression of virulence genes associated with the adherence and invasion of AIEC. Similarly, NE had a different effect on the uptake and survival of *E. coli* within macrophages.

**Conclusion**: Stress-related neuroendocrine hormone norepinephrine enhances the virulence of AIEC by increasing their adherence and invasion into the intestinal epithelium, and the expression of virulence genes.

B. Sobieszczańska: None. P. Krzyżek: None. M. Turniak: None. U. Walczuk: None.

## P3.13 | Characteristics of faecal microbiome analyses & enterotypes of healthy preschool children

**E. Micule**[1,2]; L. Lagzdina[2]; L. Broka[1,2]; A. Brumane[1]; D. Perminovs[2]; M. Gavars[2]; I. Rumba-Rozenfelde[2]; I. Daugule[2]

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**Background**: At present a lot of data show the importance of composition of gut microflora in the development of different diseases. Three different enterotypes have been identified: type 1 -*Bacteroides*, type 2 - *Prevotella*; type 3 - *Ruminococcus*.

**The purpose**: To detect the composition of intestinal microbiota in healthy preschool children. To analyze association between age and delivery type with microbial diversity & identify main enterotypes.
**Methods**: The study was performed at the children's hospital, primary health care centers, kindergartens in Latvia, including healthy infants & preschool children. Parents of children were asked to answer a questionnaire & bring a faecal sample of their child. Further, DNA was extracted from feces & sequencing of the bacterial 16S rRNA gene.
**Results**: Patient sample included 63 children; with mean age - 7,9 months. Out of them - 40 infants, 23 - preschool children. The majority of children (51) were born vaginally. *Development of* several types of microbiota could be identified among children: 66.7% (42/63) had type-1 enterotype, 27%(17/63) - type-3. Only 6.3%(4/63) resembled type-2 enterotype. Type-3 enterotype was observed more often in children born by C-section compared to children born vaginally 66.7%(8/12) *vs* 17.6%(9/51), $P = 0.001$ & among toddlers compared to infants 63%(12/19) *vs* 12.5%(5/35), $P = 0.001$.
**Conclusion**: Enterotype could be influenced by type of delivery and age. Since some data suggest that *Ruminococcus* prevalence & dysbiosis might be associated with development of different diseases, possible outcomes of early life composition of intestinal microbiota should be studied further.
E. Micule: None. L. Lagzdina: None. L. Broka: None. A. Brumane: None. D. Perminovs: None. M. Gavars: None. I. Rumba-Rozenfelde: None. I. Daugule: None.

## P3.14 | Compositional analysis of ocular surface microbiome in blepharitis

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The ocular surface is continuously exposed to environmental factors, however there is limited number of studies on ocular microbiome in health and disease status. Herein, we aimed to determine the ocular microbiome of patients with blepharitis.
In this pilot study 6 patients diagnosed with chronic blepharitis were included. Study subjects were examined using a slit-lamp biomicroscope to screen for the presence of ocular signs of blepharitis. Sampling was made using sterile swaps. After DNA isolation, amplicon libraries were prepared for V4 region and sequenced with Illumina Miseq platform. QIIME was used for preprocessing and analyzing of the data.
Our findings on 6 patients with severe blepharitis revealed a complex diverse microbiome with higher relative abundance of *Neisseria subflava*. This is an interesting finding, since none of the studies showed this bacterium in healthy ocular microbiome. With this research we will be able to test this finding in a larger population by comparing it with the healthy core ocular microbiome.
C. Ozkul: None. M. Yalinay: None. F. Akata: None.

## P3.15 | Relationship between the numbers of Candida albicans and abundance of *Helicobacter* spp. in the gut microbiota of Familial Mediterranean fever patients

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**Introduction**: Taking into account the high incidence of Familial Mediterranean fever (FMF), an autosomal recessive autoinflammatory disease, in Armenia and high levels of *Candida albicans* in the patient's gut (1), as well as the associations between the disease and *Helicobacter pylori* infections (2), we aimed to investigate the relationship between the numbers of *C. albicans* and abundance of *Helicobacter* spp. in the gut microbiota of FMF patients.
**Methods**: Forty healthy and forty-eight FMF volunteers were participated in a double blind, partly randomized, placebo-controlled trial described by us previously (1). All patients (age range: 18-50 year) used their regular colchicine medication (1 mg daily) more than 7 year.
**Results and Discussion**: The comparative investigations of FMF and healthy voluntaries revealed a statistically significant decrease in operational taxonomic units (OTUs) of several *Helicobacter* spp., including *H. cinaedi*, in FMF patients ($P < 0.01$). At the same time, there was no detectable significant difference between OTUs of *Helicobacter* spp. in male/female FMF patients as compared to *C. albicans*-carrier patients ($P > 0.05$).
According to authors, *H. pylori* may be essential bacterium colonizing human stomach (3).Most likely, another *Helicobacter* spp., might also be important for human being.
Thus, current investigations suggest that M694V/V726A pyrin inflammasome mutations may affect on helicobacter communities, independent from the high numbers of *C. albicans* in the gut microbiota of FMF patients.
1. Pepoyan A. et al. (2018) Frontiers in Immunology, https://doi.org/10.3389/fimmu.2018.0142
2. Verrecchia E. et al. (2017) Mediators of Inflammation, https://doi.org/10.1155/2017/7461426
3. Li J, Perez-Perez GI. (2018) Frontiers in Microbiology, https://doi.org/10.3389/fmicb.2018.00609.
A. Pepoyan: None. N. Harutyunyan: None. E. Pepoyan: None. V. Tsaturyan: None. T. Torok: None.

## P3.16 | The effect of conditions storage of breath samples on the hydrogen and methane levels in the SIBO diagnosis

**V. Kryvy**; I. Kliaritskaia; T. Tsapyak; Y. Rabotyagova

*Medical Academy named after S.I. Georgievsky of Vernadsky CFU, Simferopol, Russian Federation*

Normal 0 false false false RU X-NONE X-NONE /* Style Definitions */ table.MsoNormalTable {mso-style-name:"Обычная таблица"; mso-tstyle-rowband-size:0; mso-tstyle-colband-size:0; mso-style-noshow:yes; mso-style-priority:99; mso-style-parent:""; mso-padding-alt:0 cm 5.4pt 0 cm 5.4pt; mso-para-margin-top:0 cm; mso-para-margin-right:0 cm; mso-para-margin-bottom:10.0pt; mso-para-margin-left:0 cm; line-height:115%; mso-pagination:widow-orphan; font-size:11.0pt; font-family:"Calibri","sans-serif"; mso-ascii-font-family:Calibri; mso-ascii-theme-font:minor-latin; mso-hansi-font-family:Calibri; mso-hansi-theme-font:minor-latin; mso-fareast-language:EN-US;} Aims: The sensitivity of the lactulose breath test (LBT) is influenced by many factors. Possible source of variability of gas measurement is represented by the technique of breath sample storage when conducting analyzes remotely.

**Methods**: A study was conducted 30 patients with functional constipation (14F/16M, mean age 31.6 ± 6.2) who were positive for the presence of SIBO by the hydrogen (H2)/methane ($CH_4$) LBT. The test was carried out for 90 minutes. Simultaneously, two air samples were taken every 15 minutes. The first sample (RT) was stored at room temperature, the second (F) at 10 C. Samples were analyzed immediately and after 12, 24 hours, on the third day.

**Results**: The average values for the LBT amounted for H2 - 28.6 ± 12.3 ppm, for CH4 - 6.8 ± 1.8 ppm. After 12 (RT: H2levels - 27.3 ± 11.0 ppm, CH4 levels - 6.7 ± 1.4 ppm, F: H2levels - 28.2 ± 11.6 ppm, CH4 levels - 6.6 ± 1.9 ppm $P > 0.05$), 24 hours (RT: H2 levels - 23.2 ± 9.4 ppm, CH4 levels - 5.2 ± 1.1 ppm, F: H2 levels - 27.6 ± 9.4 ppm, CH4 levels - 6.3 ± 1.6 ppm, $P < 0.01$), third (RT: H2 levels - 20.3 ± 8.9 ppm, CH4 levels - 3.6 ± 0.5 ppm, F: H2 levels - 24.1 ± 10.7 ppm, CH4 levels - 6.1 ± 1.3 ppm, $P < 0.01$) day.

**Conclusions**: Simple refrigeration of breath sample is sufficient to ensure the stability of hydrogen and methane concentrations for a long time.

V. Kryvy: None. I. Kliaritskaia: None. T. Tsapyak: None. Y. Rabotyagova: None.

## P3.17 | Dysbiosis in the small intestine: Towards an optimal therapy to normalize the intestinal microbiota

**C. Mosoni**; T. Dionisi; L. Lopetuso; G. Rizzatti; A. Gasbarrini; G. Gasbarrini

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**Background**: Many studies evidenced the role of antibiotics in the modulation of Gut Microbiota (GM). Rifaximin showed its eubiotic function on GM. However, the characteristic of the GM always tends to return to its baseline characteristics.

**Aim and methods**: To define, after the pharmacological correction of intestinal dysbiosis, the proper duration of the therapy, and the proper timing for the drug re-administration. We studied 6 male and 4 female subjects with symptoms due to bacterial contamination of small intestine. The diagnosis was confirmed through lactulose H2 breath test (BT). Rifaximin was given to 5 subjects at the daily dose of 600 mg: 200 mg after each of the 3 meals, for 5 days per month. The other 5 subjects were treated with Rifaximin for two cycles of 5 days each every month. All subjects repeated the breath test after one month.

**Results**: After one month: - in 3 subjects treated with only one cycle of Rifaximin, the BT maintained its characteristics. In other 2 cases the correction was partial; - in 4 subjects treated with two cycles the BT indicated normal results; - only in one case there was an almost absent elevation of the H2

**Conclusions**: Overall, our study suggests that Rifaximin may be able to correct intestinal dysbiosis, and to maintain its outcome when administered every 15 days. Further investigation is needed on more cases, using higher doses of the drug and at different time of administration, also evaluating potential interferences and dosing CH4.

C. Mosoni: None. T. Dionisi: None. L. Lopetuso: None. G. Rizzatti: None. A. Gasbarrini: None. G. Gasbarrini: None.

## P3.18 | Lack of association between *Helicobacter pylori* infection and risk of diabetes: A cohort study

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**Background**: The aim of this study was to investigate the association between *Helicobacter pylori* (*H. pylori*) infection and the risk of type 2 diabetes, impaired glucose tolerance (IGT), diabetic nephropathy, and glycemic control.

**Methods**: We performed a retrospective cohort study of 16,091 subjects without diabetes at baseline who underwent repeated

health examinations. Subjects were categorized as seropositive and seronegative for *H. pylori* infection. Hazard ratio (HRs) and 95% confidence intervals (CIs) were calculated using Cox proportional hazard modelling. Then, we validated this serological results using an independent cohort (n = 42,351) based on histologic diagnosis of *H. pylori* infection.

**Results**: During the follow-up period of 107,809.7 person-years, 1,338 (8.3%) newly diagnosed cases of diabetes occurred. There was no statistically significant difference in cumulative incidences of diabetes between *H. pylori* seropositive and seronegative subjects. In the multivariate Cox proportional-hazards regression models adjusted for potential confounders, *H. pylori* seropositivity and diabetes (HR 1.02; 95% CI 0.89-1.16; *P*-value = 0.834), IGT (HR 0.99; 95% CI 0.94-1.05; *P*-value = 0.754), diabetic nephropathy (HR 0.99; 95% CI 0.82-1.20; *P*-value = 0.934), or glycemic control (HR 1.05; 95% CI 0.91-1.23; *P*-value = 0.496) were not significant. In concordance with serological results, the histopathological findings of *H. pylori* infection had no significant association with diabetes, its complications, or its control (*P*-value = 0.325, 0.883, and 0.975, respectively).

**Conclusion**: In this large independent cohorts study, the development, complication, or control of diabetes was not associated with *H. pylori* infection. The association between *H. pylori* infection and diabetes may have been confounded by lifestyle or metabolic factors.

J. Pyo: None. H. Lee: None. J. Lee: None. J. Kim: None. T. Kim: None.

## P3.19 | Sex differences of gut microbiota composition in C57BL/6 mice and its role in high fat diet induced metabolic disorders

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**Background**: Accumulating evidence indicates that high-fat diet (HFD)-induced metabolic disorders are associated with dysbiosis of gut microbiota. However, the relationship between gut microbiota and sexual dimorphism in susceptibility to HFD-induced metabolic disorders remains to be elucidated.

**Methods**: Male and female mice were randomly assigned to receive chow-diet (CD) or HFD for 12 weeks. Some of the mice fed on HFD were pretreated with antibiotics for 4 weeks. Body weight, insulin sensitivity and serum levels of metabolic parameters including blood glucose and insulin were evaluated. The gut microbiota of mice was characterized by 16S rRNA gene sequencing.

**Results**: HFD-induced body weight gain (BWG) in male mice was higher than those in female mice. The insulin resistance was increased in HFD group compared to CD in male mice, while there was no difference in female mice. Antibiotic-pretreatment suppressed HFD-induced BWG in female rather than male mice. The composition of gut microbiota in male mice separated from those of female mice whether fed on CD or HFD. The shannon index was reduced in HFD group compared with CD in female mice, while no difference in male at week 16. Genus *parabacteroides*, *lactobacillus* and *bifidobacterium* in female mice were markedly higher than male. Antibiotic-pretreatment significantly affected HFD-induced alterations of gut microbial communities in both female and male mice. Genus *Roseburia* and *Faecalibacterium* were increased in antibiotic-pretreated HFD compared to HFD in male and female mice, respectively.

**Conclusions**: Sex differences in HFD-induced alterations of metabolic parameters and antibiotic-induced metabolic improvement were associated with gut microbiota.

C. Peng: None. C. He: None. N. Lu: None.

## P3.20 | $^{13}$C-octanoic acid breath test is used for in-vivo diagnosis of solid-phase gastric half emptying time for gastric motility disorders

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**Introduction**: $^{13}$C-octanoic acid breath test used for in vivo diagnosis of solid gastric emptying rate and allows to detect gastric motor disorders. The $^{13}$C-octanoic acid breath test represents a novel method for the assessment of gastric emptying of solid nutrients and compares with the current standard methods (i.e. scintigraphy).

**Method**: We present two open, prospective phase III studies was aimed to validate the $^{13}$C-octanoic acid breath test(Gastromotil) for the determination of gastric emptying rate in comparison with radio scintigraphy with regard to half emptying time ($t_{1/2}$), duration of lag phase ($t_{lag}$), sensitivity, specificity, negative and positive predictive values.

**Results/Discussion**: The analysis was conducted including a total number of 226 subjects. The sensitivity and specificity of the tests were evaluated in Patients with Diabetes and GORD. Differences in the conduct and administration of the radioscintigraphy may account for this discrepancy. $t_{l/2}$ was in good agreement using the Gastromotal breath test between the two study centres, indicating that the reproducibility of this test is good. This is supported by the sensitivity and specificity of the test. For all subjects, a sensitivity of 88.4% and a specificity of 70.2% was reached. The fact that the accuracy for the $^{13}$C-octanoic acid breath test is only 80% when compared to the scintigraphic method does not impact on the high value of this test. The two methods are based on different principles; the $^{13}$C-octanoic acid breath test relies on the metabolic oxidation of the marker and the scintigraphy method on the physical processing of the radioisotope.

S. Aygen: None. M. Schmidt: None. J. Bures: None.

## P3.21 | The relations between blood leptin and *Helicobacter pylori* in schoolchildren in association with body mass index

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During the last years researchers have marked negative influence of obesity upon the formation of digestive tract pathology. Hyperleptinemia is regarded as its link.

**Aim**: To study the association between *H. pylori* and leptin, circulating in blood in schoolchildren with normal and obese indices of body mass.

**Materials and Methods**: We studied 46 gastritis schoolchildren in the ages from 7 to 17 years: with normal body mass (Cohort 1, n = 31), and obese (Cohort 2, n = 15). There was performed gastroscopy with biopsy and blood tests. *H. pylori* was identified by morphological method after Gimza coloring. Leptin content in blood plasma was determined by immune enzyme method (Human Adiponectin ELISA kit, producer BioVendor). Body mass index was calculated by the formula BMI=(kg)/Height(m)2 including the assessment with WHO percentile tables taking into account standard deviations of BMI. Inter-cohort comparison of the indices was carried out using Mann-Whitney criterion under <0.05.

**Results**: In the examined subjects of Cohort 1 with *H. pylori* the leptin level amounted 0.1 (0.1 - 3.1) ng/mL and without *H. pylori* - 0.9 (0.1- 10.2) ng/mL (=0.4175). In Cohort 2 - 17.8 (8.6 - 30.5) ng/mL and 33.5 (17.4 - 49.1) ng/mL accordingly (=0.2319). At the same time in Cohort 2 leptin level was considerably higher than in Cohort 1 in both *H. pylori* subjects (=0.0006), and in erosive lesion (=0.0167).

**Conclusion**: In *H. pylori* children the association between blood leptin level and body mass indices (normal and obese) haven't been found.

V.A. Vshivkov: None. T.V. Polivanova: None. V.V. Tsukanov: None.

## P3.22 | The change of the gut microbiota composition with regard to gastric cancer stage

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Microbiota can affect cancer susceptibility and progression by diverse mechanisms. But there has been few reports of gut microbiome change regarding to gastric cancer stage. Therefore, we compared the intestinal microbiota change in cancer stage using 16S rRNA transcript amplicon sequencing and bacteria culture method. Stool samples were collected from 26 gastric cancer patients. 16S rRNA genes from stool sample were sequenced on the Illumina Miseq platform and further analyzed to evaluate the gut bacterial community. And bacteria strains were isolated from fecal sample. In the cancer group, the relative abundance of the phylum *Firmicutes* and *Bacteroidetes* was decreased in stage IV than the other stages. Among them, the relative abundance of class *Ruminococcaceae* and genus *Bacteroides* were reduced remarkably. On the contrary, the phylum *Proteobacteria* and *Actinobacteria* were increased in stage IV. Especially, the family *Enterobacteriaceae* was observed highly in stage IV. In the bacterial culture-based approach, 40 genera including *Enterococcus*, *Clostridium*, *Bacillus*, *Lactobacillus*, *Bifidobacterium*, *Eubacteria*, *Anaerostipes* were isolated in stage I. However, only 14 genera such as *Streptococcus*, *Shigella*, *Clostridium*, *Escherichia*, *Enterococcus*, *Bifidobacterium*, and *Bacteroides* were isolated at the other stages. The microbial community in gastric cancer stage IV is characterized by the increase in the relative abundance of family *Enterobacteriaceae* of the phylum *Proteobacteria*, as well as the decrease in the relative abundance of *Bacteroides* and *Firmicutes* than those of stage I, II, III. In the cultivated method, the diversity of isolated bacteria was substantially reduced in gastric cancer stage II, III, IV than the stage I.

D. Lee: None. M. Seol: None. S. Ma: None. Y. Park: None. C. Shin: None. H. Yoon: None. N. Kim: None. J. Cho: None. S. Seol: None.

## P3.23 | Driving kimchi to ameliorate *Helicobacter pylori*-associated chronic atrophic gastritis through definite microbiota changes

**K. Hahm**[1]; Y. Shin[2]

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After our successful documentation that probiotics kimchi significantly ameliorated the development of *Helicobacter pylori*-associated chronic atrophic gastritis in mice model, probiotic kimchi also prevented *H. pylori*-associated gastric cancer via significant anti-inflammatory, anti-oxidative, and antimutagenic mechanisms. Additional study to compare the efficacy of these anti-mutageneses relevant to chronic *H. pylori* infection according to fermentation clearly concluded the fermentation to yield beneficiary microbiota was essential in these cancer preventive actions of kimchi. In this study, we performed the analysis of microbiota changes in mice and human models. After 24 weeks of *H. pylori* infection in C57BL/6 mice, the changes of microbiota were significantly correlated with the pathological conditions of stomach ($P < 0.001$ between normal and CAG; $P < 0.01$ between CAG and CAG treated with fermented kimchi). As RCT, fermented kimchi and standard non-fermented kimchi was administered to patients diagnosed with either *H. pylori* (+)/ no significant stomach pathology (24 patients) and *H. pylori* (+)/ moderate to severe chronic atrophy gastritis (24 patients). As results, significant changes in microbiota phyla were noted between *H. pylori* infection only and *H. pylori*-associated CAG and these changes were

significantly rearranged with fermented kimchi administration, signifying that chronic dietary intake of fermented kimchi can be anticipating dietary intervention against *H. pylori*-associated atrophic changes.

K. hahm: None. Y. Shin: None. S.J. Reider: None. S. Moosmang: None. L. Trgovec-Greif: None. J. Tragust: None. N. Przysiecki: None. S. Sturm: None. H. Tilg: None. H. Stuppner: None. T. Rattei: None. A.R. Moschen: None. S. Tragust: None.

## P3.24 | A prebiotic intervention with partially hydrolyzed guar gum beneficially influences intestinal microbiome composition and metabolism

**S. J. Reider**[1,2]; S. Moosmang[3]; L. Trgovec-Greif[4]; J. Tragust[1]; S. Tragust[5]; N. Przysiecki[2,1]; S. Sturm[3]; H. Tilg[2]; H. Stuppner[3]; T. Rattei[4]; A. R. Moschen[1,2]

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**Introduction**: The composition and functional properties of the intestinal microbiome are a major determinant of human health. Prebiotic intervention has the potential to modulate a dysbiotic microbiome but knowledge on the interplay of nutrition, microbiome and host physiology is still limited. PAGODA aimed to uncover mechanisms of interaction between a dietary fiber intervention (partially hydrolyzed guar gum, PHGG) and structural and metabolic properties of the intestinal microbiome.

**Methods**: A longitudinal trial with 19 healthy participants (8 male, 11 female) and a duration of 9 weeks was performed. The study included three consecutive periods of three weeks: baseline, intervention and wash-out. During the intervention period, participants received doses of up to 15 g PHGG/day. Fecal samples were collected and a questionnaire on abdominal symptoms and stool habits (based on Bristol Stool Scale) was completed every week. Fecal microbiome composition was investigated by 16S metagenomics of both the V1-V3 and the V3-V4 regions. The fecal metabolome was assessed using nuclear magnetic resonance spectroscopy (NMR). Metagenomic and metabolomic datasets were linked using sparse correlation analysis.

**Results**: PHGG intake was associated with increased stool frequency and reduced consistency (stronger effect in males; persistent during wash-out period). Alpha-diversity was transiently decreased and community composition became significantly different from the baseline during PHGG intake. Differentially abundant taxa during the intervention included *Roseburia*, *Lachnospiraceae*, *Ruminococcus and Faecalibacterium*. NMR spectra revealed a shift during intervention, mostly attributable to short-chain fatty acids.

**Conclusion**: A dietary intervention with PHGG induces beneficial changes in intestinal microbiome composition and microbiota-derived metabolites.

## P3.25 | Study of the impact of *Helicobacter pylori* eradication treatments on the intestinal microbiota

**A. G. McNicholl**[1]; S. Prast-Nielsen[2]; L. P. Andersen[3]; J. C. Machado[4]; M. Leja[5]; T. Alarcon[6]; A. Gasbarrini[7]; F. Megraud[8]; C. O'Morain[9]; L. Engstrand[2]; J. P. Gisbert[1]; On behalf of the EHMSG

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*AGM and SPN both contributed as first author. LE and JPG both as senior*

**Background**: Helicobacter pylori eradication requires a combination of antibiotics. Among the adverse events observed, intestinal disorders are frequent, especially diarrhoea, suggesting a negative effect on the intestinal microbiota.

**Methods and Aims**: Pilot study to evaluate and compare the impact of H. pylori eradication regimens on intestinal microbiota. Two 14-day quadruple treatments were evaluated: proton-pump-inhibitor and nitroimidazole plus either bismuth-tetracycline (Treatment A); or plus amoxicillin-clarithromycin (Treatment B). Stool samples were collected before, at 2 and 6 months after finishing treatment. Gut microbiome was analyzed from the stool samples by sequencing of the 16S rRNA gene and sample-specific barcode sequences. In each visit patients brought a diary registering drug intake, symptomatology and other relevant data.

**Results**: Of 50 patients were initially included and 38 completed the protocol (136 samples). 58% were women, average age was 42 years. Eradication rates were similar between treatments (A 90%, B 89%). Both treatment regimens induced a significant decrease in alpha diversity at the end of treatment, which was partially recovered in follow-up samples. Beta diversity was also similarly affected in both treatments and partially recovered at follow-up. Longitudinal pairwise Bray-Curtis distances were calculated. Large individual variation was observed ranging 0.23-0.90 during treatment and 0.18-0.77 at follow-up, in treatment A; and 0.31-0.89 and 0.27-0.92 in treatment B.

**Conclusion**: *H. pylori* eradication treatments significantly reduce microbiome diversity, although it is partially recovered soon

(<6 months) after treatment. No differences were found between bismuth and non-bismuth quadruple therapies, therefore other aspects should guide prescription.

A.G. McNicholl: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Mayoly, Allergan, Takeda, MESD. F. Consultant/Advisory Board; Modest; Mayoly. S. Prast-Nielsen: None. L.P. Andersen: None. J.C. Machado: None. M. Leja: None. T. Alarcon: None. A. Gasbarrini: None. F. Megraud: None. C. O'Morain: None. L. Engstrand: None. J.P. Gisbert: Other; Modest; Dr. Gisbert has served as speaker, consultant and advisory member for or has received research funding from Casen Recordati, Mayoly, Allergan, Advia, Diasorin.

## P3.26 | Possible links between human gut microbiota changes and adverse events during *H. pylori* eradication therapy

**D. Safina**[1]; M. Markelova[1]; S. Abdulkhakov[1,2]; T. Grigoryeva[1]; E. Boulygina[1]; D. Khusnutdinova[1]; S. Malanin[1]; I. Vasilyev[1]; M. Siniagina[1]; R. Abdulkhakov[2]

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Diarrhea is one of the most common adverse events during antibacterial therapy. However, the possible causes of diarrhea development remain unclear.

The aim of the study was to identify differences of the gut microbiota taxonomic composition initially and immediately after *H. pylori* eradication therapy depending on the presence of diarrhea during treatment.

Stool samples were collected from 102 *H. pylori*-positive patients before and immediately after eradication therapy (amoxicillin 1000 mg, clarithromycin 500 mg, proton pump inhibitor, bismuthate tripotassium dicitrate 240 mg bid for 14 days). Total DNA extracted from stool samples were sequenced on SOLiD 5500 Wildfire platform. Relative abundance of bacterial genera was evaluated in the gut microbiota before and immediately after the treatment.

Seven out of 102 (6.9%) patients had diarrhea during eradication therapy. The relative abundance of *Enterococcus* genus was significantly higher initially in patients with diarrhea during therapy compared to patients without diarrhea (0.22 ± 0.37)% vs (0.06 ± 0.21)%, $P = 0.029$. Abundances of *Collinsella* and *Lactococcus* genera were significantly higher immediately after eradication therapy in patients without diarrhea than in patients who had diarrhea during the treatment - (0.11 ± 0.43)% vs 0, $P = 0.049$ and (0.35 ± 1.53)% vs (0.01 ± 0.01)%, $P = 0.045$, respectively.

So the differences in the taxonomic composition of the gut microbiota initially and immediately after the therapy were found depending on the presence of diarrhea as an adverse event. Higher abundance of *Enterococcus* genus may probably be a predictor of the diarrhea occurrence during *H. pylori* eradication therapy. Higher prevalence of *Collinsella* and *Lactococcus* may probably indicate their protective effect from this adverse event.

D. Safina: None. M. Markelova: None. S. Abdulkhakov: None. T. Grigoryeva: None. E. Boulygina: None. D. Khusnutdinova: None. S. Malanin: None. I. Vasilyev: None. M. Siniagina: None. R. Abdulkhakov: None.

## P3.27 | Adverse events during *H. pylori* eradication therapy and human gut microbiota functional potential changes

**D. Safina**[1]; M. Markelova[1]; S. Abdulkhakov[1,2]; T. Grigoryeva[1]; E. Boulygina[1]; D. Khusnutdinova[1]; S. Malanin[1]; I. Vasilyev[1]; M. Siniagina[1]; R. Abdulkhakov[2]

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Adverse events such as diarrhea are often observed during *H. pylori* eradication therapy.

The aim of the study was to evaluate gut microbiota functional potential during *H. pylori* eradication therapy in patients with/without diarrhea as an adverse event.

Stool samples obtained from 102 patients before and immediately after eradication therapy (amoxicillin 1000 mg, clarithromycin 500 mg, proton pump inhibitor, bismuthate tripotassium dicitrate 240 mg bid for 14 days) were collected. DNA was extracted from stool samples and sequenced on SOLiD 5500xl-W. Relative abundances of metabolic pathways (MP) were classified according MetaCyc database, $P < 0.05$ was considered statistically significant.

Seven (6.9%) patients had diarrhea during eradication therapy. Abundance of 22 MP was higher initially in patients with diarrhea compared with patients without diarrhea. Most of differences were found in biosynthesis MP (14): sugar nucleotide (2), cell structure (1), ubiquinol (1), NAD (2), fatty acids (8). Less of MP were in Degradation/Utilization/Assimilation [amino acids (1), aromatic compounds (1), phosphorus compounds (1), fatty acids (1), purine (1)], Generation of Precursor Metabolite and Energy processes (2) and nucleic acid processing MP (1). Immediately after the therapy abundance of 5 MP: carbohydrate (2) and amino acid (2) biosynthesis, pentose phosphate pathway (1) was higher in patients without diarrhea. However, 4 MP: biotin biosynthesis (1), L-arginine (1) and nicotine (1) degradation, nucleic acid processing (1) were predominant after the therapy in patients with diarrhea.

So there are differences in the gut microbiota functional potential which are probably linked with the presence of diarrhea during eradication therapy.

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## P3.28 | Understanding the prebiotic potential of different dietary fibers on patients with acute pancreatitis by in vitro fecal fermentation

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**Background**: The gut failure often occurs early in acute pancreatitis (AP) and associates with the severity and outcome of disease. Accumulating evidence suggests the dysbiosis of gut microbiota in AP, yet whether the prebiotic dietary fibers play a role in restoring gut homeostasis remains controversial.

**Methods**: The fecal samples were collected from 20 patients with moderate severe acute pancreatitis. The potential prebiotic effects and fermentability of ten commonly consumed fibers were compared using an in vitro fermentation system measuring changes in fecal microbiota, total gas production and formation of common short chain fatty acids (SCFAs). Materials analyzed included: lactulose (LAU), raffinose (RAF), fructo-oligosaccharides (FOS), galacto-oligosccharides (GOS), mannan-oligosaccharide (MOS), xylo-oligosaccharides (XOS), inulin, xylitol, resistant dextrin (Rdex) and YCFA.

**Results**: The amount of SCFAs was significantly reduced in patients with AP compared to healthy subjects, and the relative abundance of *Bifidobacterium* was decreased while *Lactobacillus* was increased. After 24 hours of fermentation, Rdex had the highest production of SCFAs followed by XOS and LAU. Notably, Rdex promoted the increase of acetic acid and butyric acid, which rose up to the normal content. LAU mainly increased the content of isobutyric acid while XOS led to the increase of propionic acid. XOS resulted in a significant increase in the genus *Bifidobacterium* followed by Rdex and GOS.

**Conclusion**: The dietary fibers including Rdex, XOS and LAU were promoted the formation of beneficial SCFAs and showed potential prebiotic effects on AP, which may facilitate their application in AP treatment.

B. Yu: None. C. He: None. N. Lu: None.

## P3.29 | Compliance to probiotic therapy in irritable bowel syndrome in clinical practice: A real-life study

**M. NaPoli**; L. Laterza; V. Petito; F. Scaldaferri; E. Gaetani; A. Gasbarrini

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**Introduction**: Probiotics have been evaluated in multiple clinical trials on irritable bowel syndrome (IBS) showing efficacy on different IBS-related symptoms. Among them, the multistrain probiotic VSL#3 (manufactured by Nutrilinea Srl and distributed by Ferring SPA) has been the object in several clinical trials. However in real-life setting long term compliance could be low.

**Aims and methods**: This is a single-center, observational, prospective study to evaluate the compliance to prescription of probiotic therapy in real life and to identify factors able to influence adherence to therapy. Patients diagnosed with IBS according to Rome IV criteria and receiving a clinical prescription of VSL#3 for their IBS symptoms were evaluated for eligibility. After two months a final visit was made to assess compliance and eventual reasons for discontinuation.

**Results**: Fifty patients (mean age 41, 26% males) have been enrolled and 49 completed the planned follow up. Sixty percent of patients resulted completely adherent to therapy. Principal reasons of not adherence among the 20 patients are the price (40%), adverse events (AEs) (30%) and poor appreciation of flavour (15%). AEs were mild and they were: bloating, constipation and flatulence and completely resolved without sequelae. Sixty-two percent of patients reported overall satisfactory benefit on their IBS symptoms with the therapy.

**Conclusions**: According to our results, despite a good safety profile, 60% of patients assumed all the prescribed probiotic therapy in real life setting with reported overall satisfactory benefit. The main reasons for lack of compliance were price of the product, mild AEs and low palatability.

M. Napoli: None. L. Laterza: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Janssen. F. Consultant/Advisory Board; Modest; Actial Farmaceutica. V. Petito: None. F. Scaldaferri: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; Sanofi, Cadigroup, MSD. E. Gaetani: None. A. Gasbarrini: D. Speakers Bureau/Honoraria (speakers bureau, symposia, and expert witness); Modest; MSD, Abbvie, Gilead, Alfasigma, Biocure, Actial Farmaceutica, Sanofi, Takeda, Dicofarm.

## P3.30 | Influence of probiotic enterococci on gastrointestinal microbiome of patients with Parkinson's disease

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**Background**: The violation of the gastrointestinal microbiome (GM) in case of Parkinson's disease (PD) suggests the use of probiotics. However, the role of probiotic in the treatment of this disease remains unclear.

The aim of the study was to evaluate the effectiveness of probiotic enterococci usage as additional components of therapy of PD.

**Material/Methods**: Clinical symptoms and gut microbiota content were monitored for 80 patients with PD received only basic therapy (control group) or used additionally probiotic *Enterococcus faecium*

L3 (L3) for 20 days. Fecal samples of patients taken before and after treatment were studied bacteriologically, by qPCR and by metagenomics analysis (16S rRNA).

**Results**: The severity of neurological symptoms and constipation for PD after L3 consumption decreased. Furthermore, the following changes were detected bacteriologically and by qPCR: to reduce the number of opportunistic members of *Enetrobacteriaceae* family, *Staphylococcus sp.*, *Bacteroides fragilis*, *Fusobacteria sp.*, and Parvomonas sp. so as an increase of the content of enterococci, lactobacilli and fecalibacteria. The metagenome analysis revealed an increase in the representation of the filum *Bacteroidetess* and the family *Lachnospiracea* together with the reduction in the abundance of the families *Enterobacteriacea*, P*revotellaceae* and *Fusobacteriaceae*. In summary these changes led to the essential improvement of GM.

**Conclusion**: The changes in GM accompanied after consumption of probiotic strain L3 caused the improvement of the clinical state of the patients with PD makes. This made it possible to recommend probiotic enterococci for the treatment of this disease. The study was supported by Russian science Foundation 16-15-10085.

E. Ermolenko: None. I. Milyuchina: None. Y. Kondratenko: None. G. Alechina: None. M. Kotyleva: None. E. Goncharova: None. A. Suvorov: None.

## P3.31 | Influence of intestinal antibiotic rifaximin and probiotics on gut microbiota in patients with diverticular disease

M. N. Rustamov[1]; **N. V. Baryshnikova**[2,3]; Y. P. Uspenskiy[2,4]

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**Aim**: To evaluate efficacy of rifaximin and probiotics in patients with diverticular disease of the large bowel.

**Materials and methods**: 45 patients with diverticular disease were examined. Colonoscopy with biopsies, colonic irrigation with barium suspension, esophagogastroduodenoscopy with biopsies, abdominal ultrasonography and study of gut microflora composition were performed. Treatment included combined use of selective intestinal antibiotic rifaximin 2 tablets twice a day for seven days, probiotics containing 3,025 billion bacteria Lactobacillus bulgaricus DDS-14, Lactobacillus rhamnosus, Lactobacillus acidophilus DDS-1 and Bifidobacterium for one month, once a day.

**Results**: Microbiological studies of feces revealed a large bowel dysbiosis in all examined: an increase of the level of conditionally pathogenic microflora in 92% of cases, a decrease of the obligatory group of bacteria in 94% of cases. On the 6th-7th days of antibiotic use, conditionally pathogenic gut microflora returned to normal level in 81% of cases. Microbiological analysis of feces performed after treatment confirmed a decrease of the level of conditionally pathogenic microflora in 90% of cases to acceptable levels and an increase of the obligatory group of bacteria to normal values in 87% of patients.

**Conclusions**: Gut dysbiosis of varying degrees was revealed in all patients with diverticular disease of large bowel. Rifaximin has a high antibacterial activity against the conditionally pathogenic intestinal microflora and can be used in the treatment of such patients. Probiotics containing Lactobacillus bulgaricus DDS-14, Lactobacillus rhamnosus, Lactobacillus acidophilus DDS-1 and Bifidobacterium bifidum, can be recommended in the treatment of patients with diverticular disease of the large bowel.

M.N. Rustamov: None. N.V. Baryshnikova: None. Y.P. Uspenskiy: None.

## P3.32 | Assessing the impact of the probiotics therapy on hydrogen and methane production in patients with functional constipation

**V. Kryvy**; I. Kliaritskaia; I. Iskova; T. Tsapyak

*Medical Academy named after S.I. Georgievsky of Vernadsky CFU, Simferopol, Russian Federation*

Normal 0 false false false RU X-NONE X-NONE /* Style Definitions */ table.MsoNormalTable {mso-style-name:"Обычная таблица"; mso-tstyle-rowband-size:0; mso-tstyle-colband-size:0; mso-style-noshow:yes; mso-style-priority:99; mso-style-parent:""; mso-padding-alt:0 cm 5.4pt 0 cm 5.4pt; mso-para-margin-top:0 cm; mso-para-margin-right:0 cm; mso-para-margin-bottom:10.0pt; mso-para-margin-left:0 cm; line-height:115%; mso-pagination: widow-orphan; font-size:11.0pt; font-family:"Calibri","sans-serif"; mso-ascii-font-family:Calibri; mso-ascii-theme-font:minor-latin; mso-hansi-font-family:Calibri; mso-hansi-theme-font:minor-latin; mso-fareast-language:EN-US;} Aims: Recent studies suggested that probiotics may be an effective means for both preventing and treating small intestinal bacterial overgrowth (SIBO). However, some studies showed discordant results for their efficacy.

**Methods**: A study was conducted 30 patients with functional constipation (14F/16M, mean age 31.6 ± 6.2) who had positive hydrogen (H2)/methane (CH4) lactulose breath test LBT. Patients were divided into three treated groups (with Bifidobacterium bifidum (1), Lactobacterium acidophillum (2), Bacillus cereus (3)).

**Results**: Baseline levels of H2 and CH4 did not have significant differences between groups (1: H2 - 29.3 ± 10.1 ppm, for CH4 - 14.9 ± 1.1 ppm, 2: H2 - 28.2 ± 13.0 ppm, for CH4 - 17.3 ± 2.1 ppm, 3: H2 - 27.3 ± 12.6 ppm, for CH4 - 15.8 ± 1.6 ppm, $P > 0.05$). After 4 weeks of therapy, the most pronounced decrease in the levels of hydrogen and methane was observed in the third group groups (1: H2 - 18.5 ± 8.4 ppm, for CH4 - 10.6 ± 0.7 ppm, 2: H2 - 17.8 ± 10.2 ppm, for CH4 - 11.5 ± 1.2 ppm, 3: H2 - 16.2 ± 9.3 (in comparison with baseline $P < 0.01$ and other groups $P > 0.05$) ppm, for CH4 - 4.8 ± 2.4 ppm (in comparison with baseline $P < 0.01$ and other groups $P < 0.01$)).

**Conclusions**: The using ability a different probiotics groups, including Bacillus cereus, to reduce the level of CH4 and H2 in patients

with functional constipation will possible to significantly reduce the incidence of SIBO.

V. Kryvy: None. I. Kliaritskaia: None. I. Iskova: None. T. Tsapyak: None.

## P3.33 | Nitrofurans in correction of gut microbiota disorders

**N. V. Baryshnikova**[1,2]; Y. P. Uspenskiy[1,3]; A. Tarasova[2]; E. V. Balukova[4]; I. N. Abdurasulova[2,3]

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**Background**: Choice of effective method for correction of moderate and severe disorders of gut microbiota is an actual question for many scientists. Nitrofurans are the antimicrobial drugs that often use for gut microbiota correction. The aim: To estimate drug resistance of opportunistic bacteria to two common used nitrofurans: nifuratel and nifuroxazide.

**Methods**: 62 patients with high risk of gut dysbiosis were observed. We perform bacteriological analysis and real time PCR in stool with detection of opportunistic bacteria level for all patients. If level of these bacteria was high, we estimated them resistance to nifuratel and nifuroxazide.

**Results**: We saw that more than half of investigated bacteria were sensitive to nifuratel and most of them were resistant to nifuroxazide (Table).

**Conclusion**: We recommend using nifuratel as an more effective of nitrofurans for correction of moderate and severe gut microbiota disorders especially in case of dysbiosis associated with Enterobacter spp. (widely prevalence and highly sensitive to nifuratel).

**TABLE -** Drug resistance of opportunistic bacteria to nitrofurans

| Type of microorganism | % of patient with high level of microorganism | % of microorganisms sensitive to nifuratel | % of microorganisms sensitive to nifuroxazide |
|---|---|---|---|
| Enterobacter spp. | 35.5 (n = 22) | 100 | 0 |
| Citrobacter spp. | 4.8 (n = 3) | 100 | 0 |
| Klebsiella spp. | 4.8 (n = 3) | 0 | 0 |
| St. aureus | 9.7 (n = 6) | 100 | 0 |
| Candida spp. | 3.2 (n = 2) | 0 | 0 |
| Proteus spp. | 3.2 (n = 2) | 0 | 0 |
| E.coli with hemolytic features | 19.4 (n = 12) | 75 | 8.3 |
| E. coli lac (-) | 6.5 (n = 4) | 75 | 0 |

N.V. Baryshnikova: None. Y.P. Uspenskiy: None. A. Tarasova: None. E.V. Balukova: None. I.N. Abdurasulova: None.

## P3.34 | Circulating blood microbiome signatures in patients with liver cirrhosis and portal hypertension

**R. Gedgaudas**[1]; J. Skiecevičienė[2]; A. Franke[3]; G. Streleckienė[2]; S. Juzėnas[2]; L. Kupčinskas[4]; J. Kupčinskas[4]

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**Aim of the study**: To detect changes in circulating blood microbiome in patients with portal hypertension(PH).

**Introduction**: Studies from recent years have shown that intestinal microbiome is linked to the development of liver cirrhosis and disease related complications. In the last two years, studies have shown changes in circulating microbiome in patients with liver disease, however, circulating microbiome in patients with PH has not been assessed yet.

**Methods**: Study was conducted in Department of Gastroenterology of Lithuanian University of Health Sciences, Kaunas Clinics and included a cohort of 58 patients with liver cirrhosis and 46 healthy control (HC) subjects. 16S rRNA gene sequencing of V1-V2 variable regions was used to determine bacterial composition of blood plasma samples.

**Results**: Taxonomic composition analysis at the phylum level revealed that blood microbiome in both PH patients and HC subjects was predominated by *Proteobacteria*, *Bacteroidetes*, *Actinobacteria* and *Firmicutes*. α-diversity was not significantly different between HC and PH patients, nor between different blood compartments of PH patients. Bacterial community structure did show significant clustering between HC and PH patients. Differential abundance analysis revealed several differently abundant genera between HC and PH patient. Subgroup analysis of PH patients with different degree of PH revealed no significant differences in composition at phylum level, α-diversity or β-diversity.

**Conclusions**: Circulating blood microbiota comprises of four main phyla - *Proteobacteria*, *Bacteroidetes*, *Actinobacteria* and *Firmicutes*. Several genera were differently abundant between PH patients and HC subjects.

R. Gedgaudas: None. J. Skiecevičienė: None. A. Franke: None. G. Streleckienė: None. S. Juzėnas: None. L. Kupčinskas: None. J. Kupčinskas: None.

## P3.35 | The relationship with the presence of DNA *Helicobacter pylori* and *Escherichia coli* of the rivers in Cracow region in various seasons of years 2012-2015

M. Plonka[1]; A. Targosz[2]; W. Reczynski[3]; M. Jakubowska[4]; A. Ptak-Belowska[2]; G. Krzysiek-Maczka[2]; U. Szczyrk[2]; M. Strzalka[2]; **T. BrzozoWski**[2]

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**Background**: The fact that *H. pylori* (Hp) and its coccoid forms can survive in the river water suggests that water may be an important factor in the acquisition infection of this bacterium. Aim: To estimate in appointed seasons (winter, summer and autumn of 2012-2015) 18 physical and chemical indicators of water quality (temperature, color, turbidity, pH, conductivity at 25° C, chlorides, nitrites, nitrates, phosphates, chlorates, sulphates, free chlorine) and to investigate a relationship with the presence of Hp DNA and Escherichia coli in the tested water samples.

**Materials and Methods**: One hundred sixty samples from rivers (Raba, Dlubnia, Rudawa, Sanka) of Cracow region were tested by PCR for the presence of DNA Hp. by using the. By this method we have also identified the bacteria specific cagA. The organic compounds were analyzed by the atomic absorption spectrometry (AAS).

**Results**: In river samples DNA Hp was detected in 28 (17.3%) out of 161 samples. Hp the virulence genes cag A was present in 23 samples (14.3%). The data obtained from the tests revealed that there was a significant linear correlation between the presence of DNA Hp and Escherichia coli and the autumn season but not winter and summer.

**Conclusions**: The presence of DNA Hp in the water rivers correlated with the presence of Escherichia coli, possibly due to fecal contamination. Consumption of untreated water should be considered a risk factor for Hp infection. (supported by grant No 2011/01/B/NZ/01539)"

M. Plonka: None. A. Targosz: None. W. Reczynski: None. M. Jakubowska: None. A. Ptak-Belowska: None. G. Krzysiek-Maczka: None. U. Szczyrk: None. M. Strzalka: None. T. Brzozowski: None.

## P3.36 | Clinical significance of study of gut microflora in patients with different bowel diseases

M. N. Rustamov[1]; **N. V. Baryshnikova**[2,3]; Y. P. Uspenskiy[2,4]

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**Objective**: To evaluate diagnostic and prognostic values of studying the status of gut microflora in patients with various diseases of large bowel.

**Materials and methods**: 206 patients, including 149 - with irritable bowel syndrome (IBS), 45 - diverticular disease (DD), 12 - ulcerative colitis (UC) were examined. 149 patients with IBS - 49 predominant constipation, 58 predominant diarrhea and 42-mixed subtype were examined. Colonoscopy with biopsies, irrigoscopy, esophagogastroduodenoscopy with biopsies, abdominal ultrasonography and composition of gut microflora for all patients were performed.

**Results**: In all patients with IBS, compensated intestinal dysbiosis was revealed. Reduction of obligate bacteria in 68%, 79% and 71% of IBS subtypes was observed respectively and the increase of conditionally pathogenic intestinal microflora was revealed in 73%, 67% and 63% of mentioned IBS subtypes respectively. Microbiological study of feces revealed subcompensated intestinal dysbiosis in all patients with DD, expressed in increase of conditionally pathogenic microflora in 82%, decrease in the obligatory bacteria in 94% of cases. In patients with UC, a decompensated intestinal dysbiosis was revealed in all patients.

**Conclusions**: These results confirm that degree of severity of pathological process in large bowel is directly dependent on the severity of gut dysbiosis. Since gut dysbiosis is a trigger for the development of inflammatory processes in allergic and autoimmune diseases of the large bowel, the study of gut microbiocenosis by microbiological methods broadens the possibilities for optimizing diagnosis, possible prediction, and evaluation of the efficacy of the treatment with antibiotics and probiotics in prevention of these diseases.

M.N. Rustamov: None. N.V. Baryshnikova: None. Y.P. Uspenskiy: None.

## P3.37 | Establishment of the first stool bank in Easter Europe

**R. Nakov**[1]; I. Lyutakov[1]; V. Petkova[2]; V. Gerova[1]; R. Kaneva[2]; P. Penchev[1]; R. Vatcheva[1]; B. Vladimirov[1]; V. Nakov[1]

*[1]Queen Yoanna University Hospital, Sofia, Bulgaria; [2]Molecular Medicine Centre, Sofia, Bulgaria*

**Introduction**: For safe implementation and broader application of fecal microbiota transplantation (FMT), quality controlled stool banking is a must. Establishing a stool bank is a complex and expensive

process, making it a real challenge in a country with lower Human Development Index (HDI).

**Aims & Methods**: To establish the first stool bank in an Eastern European country – Bulgaria. A multidisciplinary team of gastroenterologists, medical microbiologists, infectious diseases specialist and geneticists was set up. We used a questionnaire based on the First European FMT Consensus in order to recruit possible stool donors. Microbiota analysis was performed on all selected donors.

**Results**: Between October 2018 and April 2019, 112 donor volunteers completed a questionnaire; 70 (62.5%) were excluded, mainly because age above 50, an unhealthy BMI and risk behavior. Forty-two (37.5%) donor candidates were invited for laboratory testing of blood and feces of which 12 (28.6%) passed this screening. Presence of *Helicobacter pylori* fecal antigen and Multi Drug Resistant Organisms were the most observed exclusion criteria. Of 12 donors, 4 (33%) failed at a following screening test, which is performed every three months. Finally, 8 (7.14%) active donors were enrolled.

**Conclusion**: Even though we found many healthy volunteers, only a low percentage (7.14%) of them are suitable to become feces donors. Establishing of a stool bank in a country with lower HDI is important for making FMT saver and more popular as a treatment method, finding further implementation and regulation of FMT and supporting physicians offering this treatment to their patients.

R. Nakov: None. I. Lyutakov: None. V. Petkova: None. V. Gerova: None. R. Kaneva: None. P. Penchev: None. R. Vatcheva: None. B. Vladimirov: None. V. Nakov: None.

## P3.38 | Donor selection experience for fecal microbiota transplantation in Brazil

D. A. A. Terra; **L. V. Coelho**; E. G. Vilela; R. O. Silva; K. S. Lima; L. A. Leao; R. I. F. A. Passos

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**Background**: Fecal Microbiota Transplantation (FMT) is a promising therapeutic option for recurrent *Clostridium difficile* infection, an increasing condition in Brazil. Despite several studies have shown similar selection programs, there is a paucity of data on screening in emerging countries. The main objective is to describe our initial experience with stool donor screening for FMT.

**Methods**: The selection was conducted prospectively in a 3-stage approach: pre-screening, clinical assessment and laboratory tests. The selection criteria were performed according to international guidelines and Brazilian epidemiological specificities.

**Results**: Over a 5-months period, 134 candidates underwent a self-survey that addressed four issues: presence of a known disease, inadequate body weight, presence of digestive complaints and logistic unavailability for donation. At this pre-screening, 101(75.7%) candidates were excluded due to at least one of these criteria. Only 33/134 candidates were considered eligible to subsequent phase. At clinical assessment, 24/33(72.7%) participants were excluded, mainly because of recent acute diarrhea, overweight (BMI > 25 kg/m$^2$) and chronic gastrointestinal disorders. Only nine participants underwent laboratory tests. Among them, five presented contraindications: positive occult blood test, free-living protozoan, *Salmonella* sp and *Isosporabelli*. Four out of 134(3%) candidates were selected after complete screening.

**Conclusion**: The appropriate selection of qualified donors is vital. Rigorous clinical evaluation allowed to identify contraindications in healthy self-reported donors before undergoing costly laboratory exams. This protocol provides subsidies for FMT in emerging countries.

D.A.A. Terra: None. L.V. Coelho: None. E.G. Vilela: None. R.O. Silva: None. K.S. Lima: None. L.A. Leao: None. R.I.F.A. Passos: None.

# POSTER ROUND 4.1 DIAGNOSIS OF HELICOBACTER INFECTION

## P4.01 | "Test and Treat" strategy with urea breath test: a cost-effective approach for the management of *Helicobacter pylori* infection in Spain

**A. G. McNicholl**[1]; P. Malfertheiner[2,3]; F. Franceschi[4]; F. Liebaert[5]; H. Salhi[5]; A. Beresniak[6]; J. P. Gisbert[1]

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**Background**: Data from clinical trials comparing strategies used for the management of dyspepsia are limited. Cost-effectiveness studies might help to identify optimal strategies.

**Aim**: To assess cost-effectiveness of the *H. pylori* "Test and Treat" strategy including Urea Breath Test (UBT) vs symptomatic treatment and/or endoscopy, in patients with dyspepsia.

**Methods**: Models compared three strategies: "Test and Treat" including UBT, "Endoscopy and Treat" and "Symptomatic Treatment". Advanced simulations were performed over 4 weeks-time horizon for the endpoint "Probability of dyspepsia symptoms relief" and over 10 years for the endpoints "Probability of gastric cancer avoided" and "Probability of peptic ulcer avoided". Models were developed according to the Spanish routine medical practices and costs.

**Results**: For the "Probability of dyspepsia symptoms relief" endpoint, "Test and Treat" was the most cost-effective (883€/success) vs "Endoscopy and Treat" and "Symptomatic Treatment" (respectively 1,628€ and 990€/success). For the "Probability of gastric cancer avoided" endpoint, "Test and Treat" was the most cost-effective strategy (524€/gastric cancer avoided) vs "Endoscopy and Treat" and

"Symptomatic Treatment" (respectively 716€ and 696€/gastric cancer avoided). For the "Probability of peptic ulcer avoided" endpoint, "Test and Treat" was also the most cost-effective strategy (421€/peptic ulcer avoided) vs "Endoscopy and Treat" and "Symptomatic Treatment" (respectively 728€ and 632€/peptic ulcer avoided).

**Conclusion**: *H. pylori* "Test and Treat" strategy including UBT is the most cost-effective medical approach for the management of dyspepsia. This study should contribute to increase awareness about the usefulness of "Test and Treat" strategy and concerning its beneficial impact for patients with *H. pylori*-related diseases.

A.G. McNicholl: F. Consultant/Advisory Board; Modest; Mayoly Spindler Laboratories. P. Malfertheiner: F. Consultant/Advisory Board; Modest; Mayoly Spindler Laboratories. F. Franceschi: F. Consultant/Advisory Board; Modest; Mayoly Spindler Laboratories. F. Liebaert: A. Employment (full or part-time); Modest; Mayoly Spindler Laboratories. H. Salhi: A. Employment (full or part-time); Modest; Mayoly Spindler Laboratories. A. Beresniak: F. Consultant/Advisory Board; Modest; Mayoly Spindler Laboratories. J.P. Gisbert: F. Consultant/Advisory Board; Modest; Mayoly Spindler Laboratories.

## P4.02 | Gastric *Helicobacter* spp. infection in a colony of research macaques: Characterization and clinical correlates

R. P. Marini; **Y. Feng**; M. M. Patterson; S. Muthupalani; A. G. Swennes; R. Ducore; H. Holcombe; M. Whary; Z. Shen; J. G. Fox

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In addition to *H. pylori*, there are non-*H. pylori* helicobacters (NHPH) that frequently colonize the stomach of nonhuman primates. *Helicobacter suis* is the predominant NHPH to inhabit the stomach of nonhuman primates and is now recognized as a zoonotic agent which has been associated with gastritis, duodenal ulcer, and gastric MALT lymphoma in humans. In this study, we evaluated the colonization of *H.suis* in rhesus macaques from a colony of animals used in cognitive neuroscience research. Animals were sampled either by gastric endoscopic biopsy, necropsy, or both. Gastric tissues were assessed histologically and evaluated by a veterinary pathologist. Gastric *Helicobacter* spp.-infection status was determined by culture, PCR and FISH. Thirteen of fifteen animals were positive for *H.suis* by PCR and FISH and two animals were also positive by PCR for *H. pylori*. Gastric biopsies from the index animal, with occasional vomiting and abdominal discomfort, were characterized as multifocal, moderate lymphoplasmacytic gastritis with intraglandular and luminal large spiral bacteria. The index and two additional animals with similar clinical signs and biopsy results were treated IM, BID with enrofloxacin (5 mg/kg), ampicillin (25 mg/kg), and famotidine (0.5 mg/kg) for 4 weeks. Their post-treatment biopsies were negative for *Helicobacter* spp. and inflammation scores of the gastric body improved from moderate to mild. *H.suis* is prevalent in captive macaques, but is associated infrequently with clinical signs, a situation akin to that of *H. pylori* infection of humans. The zoonotic potential of *H.suis*-infected macaques for researchers is likely diminished by the extensive use of personal protective equipment in the biomedical research environment.

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## P4.03 | Association of *Helicobacter pylori* with preoperative comorbidities and outcomes in bariatric surgery candidates, a retrospective study

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**Introduction**: *Helicobacter pylori* is a common gastric pathogen, typically associated with gastric pathologies but also with type 2 diabetes, obesity, cardiovascular disorders, dyslipidemia and several other comorbidities. This study aimed to assess the association of *H. pylori* with different preoperative comorbidities in bariatric surgery candidates and with weight loss following the procedure.

**Methods**: Data of bariatric surgery patients undergoing Roux-en-Y Gastric Bypass or Sleeve Gastrectomy surgery were retrospectively reviewed. *H. pylori* status was either diagnosed by histopathological staining or by a 13C urea breath test.

**Results**: 266 of 901 patients included (29.52%) were screened positive for *H. pylori.* Detection by urea breath testing was higher than by histopathology ($P < 0.003$).*H. pylori* was not associated with age, liver steatosis, dyslipidemia, or endoscopically diagnosed gastritis (table 1). In contrast, patients with *H. pylori* had a higher average preoperative BMI and HbA1c, but lower prevalence of endoscopic signs of esophagitis and lower hs-CRP levels. Preoperative *H. pylori* was associated with reduced total weight loss (%TWL, $P = 0.001$) and excess BMI loss ($P < 0.001$) 12 months after surgery. Resistance to triple therapy was 34.55%.

**Conclusion**: In this study, *H. pylori* was not associated with type 2 diabetes, dyslipidemia or liver steatosis. Significantly lower detection rates were seen with endoscopically obtained biopsies compared to a urea breath test analysis. Reduced weight loss was observed during the first 12 months after surgery.

| | *H. pylori* Screening Negative (n = 635) | *H. pylori* Screening Positive (n = 266) | *P*-value |
|---|---|---|---|
| Patient characteristics | | | |
| Mean age (years, SD) | 42.37 (13.00) | 43.68 (12.00) | 0.156 |
| Male gender (n, %) | 217 (34.17) | 105 (39.47) | 0.130 |
| Mean preop. BMI (kg/m², SD) | 41.58 (4.83) | 42.39 (5.02) | **0.025** |
| Active smoker (n, %) | 143 (22.52) | 55 (20.68) | 0.309[1] |
| Inactive smoker (n, %) | 149 (23.46) | 53 (19.92) | 0.153[1] |
| Surgical characteristics | | | |
| Gastric bypass (n, %) | 558 (87.87) | 223 (83.83) | |
| Sleeve gastrectomy (n, %) | 77 (12.13) | 43 (16.17) | 0.104[2] |
| Revision from gastric banding (n, %) | 42 (6.61) | 19 (7.14) | 0.773 |
| Open procedures (n, %) | 28 (4.41) | 11 (4.14) | 0.854 |
| Comorbidities | | | |
| Diabetes mellitus type II (n, %) | 163 (25.67) | 81 (30.45) | 0.141 |
| Mean preop. HbA1c (mmol/mol, SD) | 40.87 (11.61) | 42.84 (13.25) | **0.043** |
| Mean preop. HbA1c (%, SD) | 5.89 (1.06) | 6.07 (1.21) | **0.045** |
| Arterial hypertension (n, %) | 235 (37.01) | 96 (36.09) | 0.507 |
| Liver steatosis (n, %) | 449/594 (75.59) | 196/248 (79.03) | 0.282 |
| Mild liver steatosis (n, %) | 96 (21.38) | 41 (20.92) | 0.479[3] |
| Moderate liver steatosis (n, %) | 84 (18.71) | 39 (19.90) | 0.306[3] |
| Severe liver steatosis (n, %) | 127 (28.29) | 43 (21.94) | 0.810[3] |
| Severity not specified (n, %) | 142 (31.63) | 73 (37.24) | |
| Serum cholesterol concentrations | | | |
| Preop. total cholesterol (mg/dL, SD) | 195.66 (42.55) | 193.14 (42.19) | 0.424 |
| Preop. triglycerides (mg/dL, SD) | 164.64 (107.41) | 157.38 (111.40) | 0.368 |
| Preop. HDL (mg/dL, SD) | 49.00 (14.57) | 48.03 (13.53) | 0.358 |
| Preop. LDL (mg/dL, SD) | 113.65 (38.16) | 114.17 (38.10) | 0.853 |
| Median hs-CRP (mg/L, IQR) | 5.5 (6.52) | 5.1 (5.50) | 0.050 |
| Patients with hs-CRP ≥ 9.5 (%) | 31.45 | 22.27 | **0.009** |
| Endoscopic preop. gastritis (n, %) | 114/393 (29.01) | 47/132 (35.61) | 0.155 |
| Endoscopic preop. esophagitis (n, %) | 163/388 (42.01) | 95/131 (27.48) | **0.003** |
| Histopathological preop. gastritis (n, %) | 209/383 (54.57) | 124/127 (97.64) | **<0.001** |
| *H. Pylori* detection | | | |
| Histopathological diagnosis (n, %) | 394 (62.05) | 134 (50.38) | **0.003** |
| C13 urea breath test (n, %) | 241 (37.95) | 132 (49.62) | |
| Posto perative outcomes | | | |
| Diabetes remission (ADA criteria) | | | |
| Complete remission (n, %) | 63/118 (53.39) | 30/48 (62.50) | 0.298 |
| Partial remission (n, %) | 6/118 (5.08) | 2/48 (4.17) | 0.981 |
| % Total weight loss (%, SD) | | | |
| 1 year after surgery | 29.59 (8.62) | 27.08 (9.32) | **0.001** |
| 2 years after surgery | 27.87 (11.04) | 26.45 (9.53) | 0.335 |
| Absolute weight loss (kg, SD) | | | |
| 1 year after surgery | 35.35 (11.17) | 32.95 (12.84) | **0.020** |
| 2 years after surgery | 33.15 (14.41) | 31.16 (13.29) | 0.308 |

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## P4.04 | A prospective and comparative study to validate the $^{13}$C-urea breath test to diagnose *H. pylori* infection using the same protocol for two different devices

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**Introduction**: 13C-urea breath test (UBT) is the gold-standard method for *H. pylori* (HP) diagnosis. However, there is no uniform standardization of the test. This situation can be unpractical for laboratories running with two or more devices.

**Aim**: To perform a prospective comparison validation study of UBT employing one validated protocol for two different devices (BreathID Hp Lab System® (Exalenz Bioscience Ltd, Israel) and IRIS-Doc 2® (Wagner Analysen-Technik, Germany, now Mayoly Spindler Group, France) in the diagnosis of HP infection.

**Methods**: 518 consecutive patients (365 females, mean age 53 years) referred for UBT were included. All patients received BreathID Hp Lab System protocol as follow: after at least one hour fasting, patients filled 2 bags prior to the test, then ingested an aqueous solution containing 75 mg of 13C-urea with a 4.0 gram citric acid powder and filled another 2 bags 15 minutes after ingesting the test solution. One pair of breath sample bags (before and after ingestion) was analyzed by the two different devices. A delta over baseline (DOB) ≥ 5‰ indicated HP infection. Statistics: Wilcoxon test, Kappa coefficient with 95% CI.

**Results**: See Table. Considering the gold standard, IRIS device showed 99.3 sensitivity (95%CI: 963-99.9) and 98.9% specificity (95% CI: 97.3-99.6). Kappa coefficient was 0.976 (95% IC: 0.956-0.997).

**Conclusions**: Correlation between the two devices was excellent and supports a uniform standardization of UBT.

**TABLE** - UBT results employing two different devices with a unique protocol (n = 518)

| Descriptive statistics (DOB ‰) | BreathID Hp lab system® | | IRIS DOC-2® | |
|---|---|---|---|---|
| | Negative | Positive | Negative | Positive |
| Mean value | 0.4 | 44.8 | -0.1 | 44.6 |
| Standard deviation (SD) | 1.0 | 26.9 | 1.5 | 26.7 |
| Median value | 0.4 | 39.4 | -0.1 | 40.4 |
| Min. value | -1.0 | 5.6 | -7.0 | 5.1 |
| Max. value | 4.9 | 119.1 | 3.9 | 123.8 |

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## P4.05 | Prevalence and risk factors associated with *Helicobacter pylori* infection among asymptomatic subjects in east, west and south of Libya

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**Background**: *Helicobacter pylori* (*H. pylori*) is the commonest global chronic infection. The difference in *H. pylori* epidemiology various between the countries, within the country likely to occur. Limited data available regarding the seroprevalence of *H. pylori* and associated risk factors in Libyan healthy population.

**Aims**: To estimate the prevalence and risk factors for *H. pylori* infection in a cohort of asymptomatic adult community in West, East, and South of Libya.

**Materials and Methods**: Totally, two hundred and fifty one healthy between 18 and 45 years, were invited to participate this study, who lived in East, West and South of Libya. A blood samples were collected, and questionnaire completed to evaluate risk factors. *H. pylori* serostatus was evaluated by use of a commercial ELISA for anti-*H-pylori* IgG.

**Results**: The overall prevalence of *H. pylori* was (51.5%). High prevalence detected in the south population (57%), compare to (39%), (31%) of the healthy participant from West and East respectively. There was a steady increase in seroprevalence with increasing age. No significant relationship found between gender**.** A significant relationship detected between *H. pylori* and O and A blood group.

**Conclusions**: Despite there are difference between East, West and South of Libya with regard to ethnic, diet and habits, the Seroepidemiology of *H. pylori* among Healthy population had a significantly higher in the south. In the three communities, risk of *H. pylori* seropositivity was related to socioeconomic, lifestyle, & environmental factors, family history of gastric disease. Further studies with more participants are required to confirm our study findings.

E.Z. Younis: None.

## P4.06 | Efficacy assessment of a new RUT

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In accordance with the Florence Consensus, rapid urease tests are recommended as the first-line tests for HP diagnosis. It is necessary to evolve diagnostic tools since the patient's treatment strategy depends on RUT's result. We combined the latest state of art materials and designed a RUT of a new generation - AMA RUT Pro. The test-system has an innovative multilayer design comprising a special membrane. It separates the enzymatic reaction layer from the indicator layer so that the reaction with *H. pylori* urease and the

following indicator reaction were not mixed. The aim of the study was to assess diagnostics efficacy of a new rapid urease test AMA RUT Pro.

**Materials and methods**: For the included patient, two biopsy specimens were taken during the endoscopic procedure: one from the antrum and one from the corpus and were placed into AMA RUT Pro. Additionally, Both PCR and Histology were used for confirmation of each result.

**Results**: The study was conducted at the site of Mariinsky Hospital in 2018. The efficacy assessment was based on the results of 376 biopsies. The AMA RUTs Pro identified HP in 136 samples, 134 of them were confirmed by both additional methods. Infection was not detected by RUTs in 240 cases and only 3 of them were a false negative. Thus, AMA RUT PRO has high specificity (98.76%) and sensitivity (99.25%).

**Conclusion**: Thanks to its' innovative design, AMA RUT Pro is fast and convenient and demonstrated high diagnostics efficacy.

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## P4.07 | Evaluation of gastric mucosal changes and pepsinogen serum levels in *Helicobacter pylori*histology and serology discrepant cases

**S. Skrebinska**[1,2]; F. Mégraud[3,4]; I. Daugule[1,5]; D. Santare[1,5,6]; S. Isajevs[1,5,7]; I. Liepniece-Karele[1,7]; D. Rudzite[1,6]; I. Kikuste[1,5,8]; A. Vanags[1,8]; I. Tolmanis[8]; J. Atstupens[1]; J. Y. Park[9]; R. Herrero[9]; C. Alix[3,4]; M. Leja[1,5,6]

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**Aim**: To evaluate presence of gastric mucosal atrophy and intestinal metaplasia in *H. pylori* serology and histology discrepant cases.

**Methods**: Individuals with positive-serology, but negative-histology and negative-serology, but positive-histology were selected from a GISTAR pilot-study database. Antibodies to *H. pylori*, pepsinogen levels were assessed in plasma by enzyme-linked immunosorbent assay (ELISA). If pepsinogen (Pg) PgI/PgII ratio was ≤ 3.0, participants were classified as individuals with decreased Pg level. Presence of gastric atrophy was evaluated according to the OLGA (Operative Link for Gastritis Assessment) system, subjects with stage III or IV were considered as group with severe gastric mucosal atrophy. Meanwhile intestinal metaplasia (IM) was evaluated according OLGIM (Operative Link on Gastric Intestinal Metaplasia Assessment) system and subjects with stage equal or greater than III were classified as group with severe IM. *H. pylori* deoxyribonucleic acid (DNA) detection in frozen biopsy sample was performed using a real-time polymerase chain reaction(PCR).

**Results**: The final patient sample for analysis contained data from 97 individuals: serology-positive/histology-negative cases were 81, serology-negative/histology-positive - 16. Majority of decreased pepsinogen I/II ratio levels were in first group with PCR negative results, of which four had gastric atrophy and three subjects - intestinal metaplasia.

**Conclusion**: Majority of OLGA and OLGIM stage III/IV gastritis was observed in a group with serology positive/histology negative cases, thus indirectly suggesting that *H. pylori* could had disappeared after causing gastric atrophy.

**TABLE.** Pepsinogen serum levels and gastric mucosal atrophy evaluation in *H. pylori* discrepant cases.

| | | Number of cases (%) | Decreased PgI/PgII | OLGA III/IV (%) | OLGIM III/IV (%) | OLGA III/IV and OLGIM III/IV |
|---|---|---|---|---|---|---|
| Serology positive, histology negative cases | PCR positive | 17/81 (21.0) | 2 | 3 (17.7) | 2 (11.8) | 2 |
| | PCR negative | 64/81 (79.0) | 11 | 4 (6.2) | 3 (4.7) | 3 |
| Serology negative, histology positive cases | PCR positive | 15/16 (93.8) | 1 | 0 | 0 | 0 |
| | PCR negative | 1/16 (6.2) | 0 | 0 | 0 | 0 |

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## P4.08 | Prevalence of *Helicobacter pylori* infection among healthy students of medical professionals

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**Background**: *Helicobacter pylori* (*H. pylori*) infection is primarily acquired during childhood, with a higher frequency in developing countries. There is no information available regarding the prevalence of *H. pylori* infection in healthy medical students population of our country.

**Objectives**: To establish seroprevalence of *H. pylori* infection in asymptomatic students of Medical Professionals in two different geographic area & its associated risk factors.

**Material and Methods**: A Blood sample from (199) young adult healthy Students (99 Females, 100 Males mean age 22 years) were enrolled, (99) from Ibn-Nafes Medical Institute, Tripoli. & (100) from Faculty of Medical Technology, Zawia University. Specific anti-*H. pylori* IgG, & questionnaire covering Sociodemographic variables were administered and completed by interview.

**Results**: Seroprevalence of *H. pylori* was (67.4%) & (39%) healthy students of Tripoli and Zawia respectively, there was a gradual increase with age, In Tripoli, females shows higher prevalence than in Zawia. In both community prevalence was higher of family members of 5-7 persons. The prevalence significantly differ by source of water drinking. However the prevalence did not significantly differ by the Blood group, smoking, hand washing, abdominal pain, and drinking Coffee or Tea.

**Conclusions**: *H. pylori* are highly among the healthy Medical students in the urban & rural community of Libya of aged 22-23 years, which might be related to the socioeconomic status, living conditions & the source of water, as a major risk factors for *H. pylori* infection. However, further studies in large group of healthy population should be conducted to confirm the study findings.

## P4.09 | Serology as a first-line diagnostic tool for *Helicobacter pylori* infection and associated acute inflammation of the stomach: possibility or reality? A retrospective study on 524 patients

**A. Barchi**[1]; M. Franceschi[2]; M. Russo[1]; M. Picchio[3]; C. Miraglia[1]; A. Ferronato[2]; K. Rodriguez-Castro[2]; M. P. Panozzo[4]; A. Antico[4]; G. Baldassarre[2]; L. Franzoni[1]; P. Crafa[1]; F. Di Mario[1]

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**Background and aim**: *Helicobacter pylori* (H.p.) is recognized as first-class carcinogen for gastric neoplasia. Pepsinogen II (PGII) and IgG anti-H.p. are markers related to infection. Aim of this study is to confirm clinical usefulness of PGII and IgG as first-line tool for diagnosis of H.p., assessing cut-off values.

**Material and Methods**: Overall, 524 patients (F: 374; Mean Age: 53 ± 16.1; Range: 14-90;) performed an $^{13}$C-UBT test or an EGD with biopsies. Everyone underwent also serology (ELISA), detecting PGI, PGII, G-17 and IgG anti-H.p.. Patients <18 years, previously eradicated or on PPI, NSAIDs, low-dose ASA were excluded. Patients with Chronic Atrophic Gastritis (OLGA staged) were included. Pearson Bivariate Correlation for IgG and PGII compared to H.p. status, T-student Distribution test, Univariate ANOVA test, ROC curves with Youden's Index J, to state specificity and sensibility of these markers to assess the infection and to set cut-off values, were used. Results were considered statistically significant for $P < 0.05$.

**Results**: $^{13}$C-UBT or EGD identified 2 groups: Group 1 141 pts (26.9%) H.p.+ (F:99; Mean Age: 51.7 ± 16; Range: 14-90) and Group 2 383 pts H.p.- (73.1%) (F:275; Mean Age: 53.5 ± 16; Range: 15.6-89.6)(Table 1.).

**Conclusions**: Prevalence of infection is 26.9%. IgG and PGII showed significant correlation, being higher in H.p.+ and lower in H.p.- group. Specificity and sensibility of PGII and IgG suggest the possibility to use serology as first-line diagnostic tool for H.p..

| | Group 1 (H.p.+) | Group 2 (H.p.-) | Youden Index J | Sig. of ROC curve | Sig. of Combined ROC IgG-PGII | Cut-off | Sensitivity | Specificity |
|---|---|---|---|---|---|---|---|---|
| IgG (EIU) ($P < 0.001$) | m.v. 12.3 ± 12.1 EIU | m.v. 91.4 ± 40.9 EIU | 0.8635 | $P < 0.001$ | $P < 0.0001$ | >25.6 EIU | 95.74% | 90.6% |
| PGII ($P < 0.001$) | m.v. 7.1 ± 3.4 μg/L | m.v. 13.9 ± 9.5 μg/L | 0.4690 | $P < 0.001$ | $P < 0.0001$ | >9.1 μg/L | 65.96% | 80.94% |

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## P4.10 | Routine detection of *Helicobacter pylori* from stomach biopsies of patients - Restructuring from culturing to molecular methods

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**Introduction**: *Helicobacter pylori* colonize the human stomach and is related to peptic ulcers, dyspepsia and gastric cancer. At our hospital, biopsies from patients with dyspepsia are cultured for *H. pylori*. It can take several days to obtain colonies of *H. pylori* due to its specific growth requirements, coccoid formation and slow growth rate. Molecular methods such as PCR are increasingly used in diagnostics due to their growth-independency and fast results.

**Objectives**: The aim of this study was to compare the number of biopsies positive for *H. pylori* by culturing and PCR with the ambition to restructure the routine analysis of biopsies to a screening by PCR.

**Materials and Methods**: DNA was extracted from stomach biopsies obtained from the routine analysis by DNeasy Blood &Tissue Kit. PCR was performed with *Helicobacter*-specific primers from the literature. The *Helicobacter*-positive samples were included in a qPCR for simultaneous detection of *H. pylori* and point mutations causing clarithromycin-resistance.

**Results**: The PCR assay was performed on a total of 346 biopsies, where 45 (13%) were positive for *Helicobacter* species, of which 35 (77%) were identified as *H. pylori* and 2 (4%) as non-*pylori Helicobacter* (8 biopsies have not yet been tested). By culturing of 350 biopsies, 21 (6%) were positive for growth of *H. pylori*.

**Conclusion**: The PCR assay shows great potential for routine detection of *H. pylori* from biopsies compared to culturing. The method can be used as a screening followed by culturing of the positive biopsies to obtain isolates for antibiotic susceptibility testing.

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## P4.11 | The accuracy of ammonia breath test for the diagnosis of *Helicobacter pylori* in dyspeptic children and adult patients

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**Background**: *Helicobacter pylori* (*H. pylori*) is common and still one of the most frequent bacterial infections in developing countries, as one of a noninvasive tests for *H. pylori* infection, Urea Breath test have been widely used worldwide. However is not common use in Libyan gastroenterology practice. Objective

To evaluate the performance of Ammonia Breath test for the diagnosis of *H. pylori* infection in symptomatic child & adults subjects attending gastroenterology Department, Tripoli Cental Hospital& Tripoli Children Hospital.

**Materials & Methods**: From June 2016 to December 2018, Six hundred dyspeptic child & adult patients (250 men and 350 women, mean age 28 years), underwent upper endoscopy with gastric biopsies for recurrent abdominal pain, vomiting, chronic diarrhea, and anemia. None had received antibiotics, antacid, and proton pump inhibitors in the preceding four weeks. Two diagnostic methods were used: The Ammonia Breath Test ("Helic- test", Association of Medicine and Analytic, St- Petersburg), & the Histological method used as a comparison method.

**Results**: By "Helic- test" the positive result was received in 79% of dyspeptic patients, and by using the histological method *H. pylori* was defined in 81% among the study subjects.

**Conclusions**: As in our study in 2017. A high coincidence of the two methods was found. In our population, the Ammonia Breath Test ("Helic- test") shows a high clinical efficiency and accuracy for the initial detection of *H. pylori*, also for the follow-up treatment diagnosis of *H. pylori* in child & adult dyspeptic patients.

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## P4.12 | *Helicobacter pylori* positivity assessed by molecular-biology methods in gastric biopsy samples in serology and histology discrepant cases

**S. Skrebinska**[1,2]; F. Mégraud[3,4]; I. Daugule[1,5]; D. Santare[1,5,6]; S. Isajevs[1,5,7]; I. Liepniece-Karele[1,7]; D. Rudzite[1,6]; I. Kikuste[1,5,8]; A. Vanags[1,8]; I. Tolmanis[8]; J. Atstupens[1]; J. Y. Park[9]; R. Herrero[9]; C. Alix[3,4]; M. Leja[1,5,6]

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**Aim**: To evaluate the presence/absence of *H. pylori* by molecular methods in subjects with discrepant histology and serology result.

**Methods**: Individuals with discrepant serology/histology results were selected from a GISTAR pilot-study database. Subjects having received *H. pylori* eradication therapy in life-time or reporting use of proton pump inhibitors, antibacterial medications, bismuth containing drug use one month prior upper endoscopy were excluded. Antibodies to *H. pylori* were assessed in plasma by enzyme-linked immunosorbent assay (ELISA). *H. pylori* deoxyribonucleic acid (DNA) detection in frozen biopsy sample was performed using a real-time polymerase chain reaction (PCR) as a gold standard. Immunohistochemistry (IHC) was performed in subjects with positive-histology and negative-serology. Presence of inflammation was evaluated according to mucosal neutrophil infiltration, subjects with stage II or III in any of biopsies was considered as a group with inflammation, meanwhile 0 or I in all biopsies - as group without inflammation.

**Results**: The final patient sample for analysis contained data from 97 individuals: serology-positive/histology-negative cases: 81, serology-negative/histology-positive: 16. Among the first group there were approximately one fifth (21.0%) falsely positives by serology, while in the second group there were 6.2% false positives by histology. In the PCR positive group six of 15 (or 40%) gastric mucosa showed no inflammation in all biopsies, but the majority (14 subjects) had ICH positive results.

**Conclusion**: Among this high *H. pylori* prevalence middle-aged population, the majority of discrepant cases between serology and histology were rather due to false positive-serology than false-negative histology. This could be explained by possible loss of bacterium due to atrophic changes in mucosa.

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## P4.14 | Comparative evaluation of efficiency of test systems for the diagnosis of *H. pylori* urease in the stomach

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**Objectives**: Evaluate the efficiency of using Jatrox-H.p.-Test, Helpil-Test, AMA RUT Pro test systems for the diagnosis of *H. pylori* (Hp) urease in the gastric mucosa in patients with dyspepsia syndrome.

**Materials and methods**: Blind, diagnostic, cross-section study of 144 patients (the mean age 40.2 ± 11.4 years, 81 men and 63 women) with application of Latin square (table 2x2) for evaluation of efficiency of rapid urease tests was carried out (AMA RUT Pro, and Helpil-Test, AMA LLC, Russia, and Jatrox-Hp-Test, Rohm Pharma, Germany). *H. pylori* was detected in the stomach by the morphological method in 79 (54.9%) people.

**Results**: Results of comparative evaluation of efficiency of the rapid urease tests (examination of *H. pylori* by Giemsa as comparison method; AMA RUT Pro, Helpil-Test, Jatrox-H.p.-Test respectively): sensitivity (Se) - 0.99; 0.97; 0.98; specificity (Sp) - 0.98; 0.98; 0.98; prevalence (P) - 0.55; 0.55; 0.55; test accuracy (TA) - 0.99; 0.97; 0.98; negative predictive value (-PV) - 0.98; 0.96; 0.98; positive predictive value (+PV) - 0.99; 0.98; 0.98; positive likelihood ratio (LR+) - 66.0; 48.5; 49.0; negative likelihood ratio (LR-) - 0.01; 0.03; 0.02.

**Conclusion**: AMA RUT Pro has high clinical efficacy for the diagnosis of *H. pylori* in the gastric mucosa. The AMA RUT Pro and Helpil-Test, respectively, reduce the time to diagnose Hp infection by a factor of 288 and 480 compared with Jatrox-H.p.-Test and allow further use of gastrobioptat for morphological research.

M.R. Konorev: None. R.A. Pavlyukov: None. M.V. Sazonov: None.

# POSTER ROUND 4.2 EPIDEMIOLOGY

## P4.15 | Prevalence, clonal distribution, and risk factors of *Helicobacter pylori* infection in tropical Africa: An assessor-blinded molecular epidemiological study

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**Aim**: In a cross-sectional study, we determined by a non-invasive genotyping method the prevalence and clonal distribution of *Helicobacter pylori* within a rural community in Central African Gabon in order to identify risk factors of *H. pylori* infection in a high transmission setting.

**Methods**: A total of 503 inhabitants from a small community near Lambaréné agreed to participate by written informed consent. Demographic characteristics, family relationships, living conditions, behavioural risk factors of the participants as well as geographic data were recorded. The genotyping method was based on single nucleotide polymorphisms in variable regions of two *H. pylori* specific sequences of the *glmM* and *recA* genes using stool specimens. Infection was determined by the antigen test and three FRET real-time PCRs targeting *glmM*, *recA* and 23S rRNA, the latter allowed also for clarithromycin susceptibility testing. Results

439 of the participants (87.3%) were *H. pylori* infected; the 23S rRNA real-time PCR was positive in 406 (92.5%) of which 40 (9.8%) harboured the clarithromycin resistant genotype. Logistic regression analysis revealed that of all analysed features only bed-sharing and the presence of a refrigerator was significantly associated with

*H. pylori* infection in a negative and positive manner, respectively. The genotyping method determined 29 clonal lineages; however, clonal distribution did not allow for a conclusive identification of origins of the infection and modes of transmission.

**Conclusion**: This epidemiological survey in a high prevalent area revealed that factors related with living conditions and the socioeconomic status rather than intra-familial relationships are associated with *H. pylori* infection.

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## P4.16 | Incidence of gastric pathology in American Indian/Alaska Native individuals with and without documented *Helicobactor pylori* infection, 2001-2014

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**Background**: *Helicobacter pylori*(Hp) infection and gastric cancer (GCan) are very common in the American Indian/Alaska Native (AI/AN) population. The Indian Health Service (IHS) system supports medical care for AI/AN people in the United States. They maintain a database with all inpatient and outpatient International Classification of Disease (ICD) codes. We used the IHS database to evaluate the diagnosis of gastritis, ulcer disease, and GCan in AI/AN people with documented Hp infection (dHp) and those without any Hp documented (uHp).

**Methods**: Individuals ≥18 years of age who received care in the IHS system in 2001 were divided into dHp and uHp based on the presence of an Hp ICD code at any time between 2001 and 2014. The age-adjusted diagnosis rates of gastritis, ulcer disease, and GCan between 2002 and 2014 were compared between the two groups. Rate ratios (RR) and 95% confidence intervals (CI) between the dHp and uHp groups were calculated using Poisson regression.

**Results**: The total population included 641,327 adults, of which 56,563 (8.8%) were dHp. The dHp group had significantly higher diagnosis rates for gastritis (RR 3.6 CI: 3.5-3.6), ulcers (RR 4.1 CI: 4.0-4.2) and GCan (RR 2.4 CI: 2.2-2.7) than the uHp group.

**Conclusions**: This investigation confirmed that individuals with documented Hp are more likely to be diagnosed with GCan, gastritis, and all ulcer types. Further analysis is being performed to identify other diagnoses related to an increased risk of GCan in this population.

L.D. Nolen: None. S. Seeman: None. J. McCollum: None. M.G. Bruce: None.

## P4.17 | *Helicobacter pylori* recurrence and its risk factors in China: A large-scale multicenter, prospective and retrospective study

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**Background & aims**: *Helicobacter pylori* (*H. pylori*) infection currently remains a significant public health concern around the world. One of the main causes is the *H. pylori* recurrence, which includes recrudescence and reinfection. The aim of this study was to evaluate the recurrence and its risk factors on a large-scale multicenter basis in China.

**Methods**: Eighteen centers use a set of standardized protocols. Data of consecutive patients with eradication for *H. pylori*-related diseases between January 2016 and December 2018 were collected prospectively. In addition, patients who had been successfully eradicated were retrospectively followed up by telephone interview. Potential factors associated with recurrence were preliminarily estimated by the log-rank test. Related risk factors for recurrence were evaluated ulteriorly by Cox regression models and showed with the Kaplan-Meier curve.

**Results**: A total of 2010 subjects with 2391 person-years of follow-up in the prospective group and 3528 subjects with 3908 person-years of follow-up in the retrospective group were included in the study. Reignition rate of *H. pylori* in China was 6.14%, annual recurrence rate and annual reinfection rate were 4.05% and 1.87%, respectively. There are six risk factors related to the recurrence of *H. pylori*, including the geographical area, antibiotic combination, combination regimes, ethnic division, education level and family history of gastric cancer (all $P < 0.05$).

**Conclusions**: The annual recurrence rate of *H. pylori* in China is 4.05%. Related risk factors are a geographical area, antibiotic combination, combination regimes, ethnic division, education level and family history of gastric cancer.

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## P4.18 | Association between decreased level of pepsinogen with different dietary factors and *Helicobacter pylori* seropositivity

**J. Aleksejeva**[1]; D. Razuka-Ebela[1,2]; I. Daugule[1,2]; I. Polaka[2]; S. Parshutin[2]; D. Santare[1,2]; I. Ebela[1]; R. Murillo[3]; R. Herrero[3]; J. Park[3]; M. Leja[1,2]

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**Introduction**: Development of gastric atrophy leading to gastric cancer is related to *Helicobacter pylori (H. pylori)* and, possibly, exposure to some dietary factors.

**Objective**: To analyze an association between decreased Pepsinogen (Pg) level, *H. pylori* seropositivity and dietary factors.

**Material and methods**: From country population register people were randomly chosen (within GISTAR pilot study), answered to a questionnaire, donated a blood sample. PgI, PgII were tested by latex-agglutination test, *H. pylori*-by ELISA. The consumption of different dietary products, alcohol, smoking status was compared between participants with normal and decreased Pg level (PgI/PgII ≤ 3 and PgI ≤ 70 ng/mL). Statistical analyses included $\chi^2$ test, logistic regression.

**Results**: Total patient sample included 1725 persons (mean age 51.62; SD ± 6.741). Decreased Pg level was observed in 32.4%(559/1725) of participants and was associated with age ≥ 51 year ($P < 0.001$). Decreased Pg level was inversely associated with the consumption (≤2 per month vs ≥ 1 a week) of sour dairy products ($P = 0.02$), cheese/cheese products ($P = 0.03$), leek ($P = 0.02$). In multivariate analysis seropositive *H. pylori* status (OR = 3.398; 95%CI:2.597-4.446), age ≥ 51 years (OR = 1.590; 95%CI:1.269-1.992), alcohol consumption (OR = 1.295; 95%CI:1.023-1.639), present smoking (OR = 1.439; 95%CI:1.105-1.872) had positive association with decreased Pg level; an inverse association was found with higher consumption of cheese/cheese products (OR = 0.045; 95%CI:0.520-0.993) and leek (OR = 0.804; 95%CI:0.633-1.021).

**Conclusions**: *H. pylori* seropositivity, advanced age, alcohol consumption, present smoking were independently linked to decreased pepsinogen level, while higher consumption of cheese/cheese products and leek were inversely associated with decreased pepsinogen level. Thus, suggesting that *H. pylori* and age play the major role in the development of atrophy.

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## P4.19 | Social inequity, gender and *H. pylori* infection in Arctic Canada

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*Helicobacter pylori (Hp)* infection has an elevated prevalence in northern Indigenous communities in Canada. This analysis investigates social inequities in the *Hp*-associated disease burden within Indigenous communities in the Northwest Territories and Yukon. We examined how deprivation indicators relate to this disease burden, with particular interest in households headed by non-partnered women relative to other households.

We used data generated by Canadian North *Helicobacter pylori* (CAN*Help*) Working Group community projects, conducted to address community concerns about *Hp*-associated risks. We estimated the Canadian Deprivation Index (CDI), a validated predictor of health status, from its 3 components: home ownership; education; and food security. We ascertained most variables by interviewing participants as they enrolled in community projects during 2007-2017; we ascertained food security in a subset of participants during 2017-2018, using the Canadian Government Household Food Security Survey, adapted for Arctic communities. As a disease burden variable, we used the prevalence of *Hp* infection based on urea breath test screening.

We had CDI data for 264 participants, 70 of whom lived in households headed by unpartnered women. *Hp* prevalence was higher among participants at higher deprivation levels, particularly for households headed by unpartnered women (see table). While severe food insecurity was rare, it was strongly associated with *Hp* prevalence. Thus, the *Hp*-associated disease burden seems related to social and gender inequities within Indigenous communities in Arctic Canada.

| | All households | | | | Households led by unpartnered women | | | |
|---|---|---|---|---|---|---|---|---|
| CDI Score | n | Hp+ | Odds ratio [95% CI] | | n | Hp+ | Odds ratio [95% CI] | |
| 1 | 47 | **32%** | 2.0 | [0.9, 4.5] | 6 | **33%** | 4.2 | [0.5, 33] |
| 2 | 78 | **19%** | 1.0 | – | 28 | **10%** | 1.0 | – |
| 3 | 61 | **46%** | 3.6 | [1.7, 7.6] | 17 | **65%** | 15 | [3.2, 73] |
| 4 | 56 | **50%** | 4.2 | [1.9, 9.1] | 11 | **64%** | 15 | [2.6, 81] |
| 5 | 22 | **45%** | 3.5 | [1.3, 9.6] | 8 | **50%** | 8.3 | [1.3, 52] |
| Total | 264 | **35%** | | | 70 | | | |

| | All households | | | Households led by unpartnered women | | |
|---|---|---|---|---|---|---|
| CDI Score | n | Hp+ | Odds ratio [95% CI] | n | Hp+ | Odds ratio [95% CI] |

CDI Score: 1 =east deprived; 5 = most deprived

| | All Households | | | | Households led by Unpartnered Women | | | |
|---|---|---|---|---|---|---|---|---|
| Food Security | n | *Hp+* | Odds Ratio [95% CI] | | n | *Hp+* | Odds Ratio [95% CI] | |
| Never insecure | 227 | **34%** | 1.0 | – | 57 | **20%** | 1.0 | – |
| Sometimes insecure | 32 | **38%** | 1.2 | [0.5, 2.6] | 8 | **38%** | 1.1 | [0.2, 5] |
| Often insecure | 11 | **91%** | 20 | [2.5, 158] | 5 | **80%** | 7.4 | [0.8, 71] |

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## P4.20 | Detection of *Helicobacter pullorum* in commercial chicken meat samples

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*Helicobacter pullorum* is considered an emerging pathogen, associated with infectious diarrhea. Chicken meat has been suggested to be an important source of transmission for *H. pullorum*, although the risk of exposure is not well known. Thus, our aim was to determine the prevalence of *H. pullorum* among chicken products for human consumption in Valencia, Spain. Forty chicken pieces (twenty four livers, ten breasts and six gizzards) were collected from different local butchers. Briefly, 10 g were enriched in 90 mL of Brucella broth at 37°C for 48 hours, under microaerophilic conditions. Then, 100 µl were filtered through 0.45 µm cellulose membrane, the filter was placed onto Columbia agar with 5% sheep blood, and incubated 30 minutes at room temperature. Finally, the filters were removed and the plates were incubated at 37°C for 48 hours under microaerophilic conditions. For each sample, aliquots of the broth, directly and after 48 hours enrichment, were analyzed by PCR. The presence of *H. pullorum* colonies in mixed cultures was also determined by PCR.

*H. pullorum* was detected by PCR in sixteen samples after 48 hours enrichment (40%). Eight of these sixteen positive samples were also positive by culture. However, five positive liver samples by culture were negative by PCR, probably due to the presence of PCR inhibitors in the sample. According to our results, *H. pullorum* is highly prevalent in our geographical area. Direct PCR after 48 hours enrichment can be a valid method to detect *H. pullorum* from chicken meat.

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## P4.21 | Comparison of prevalence *H. pylori* infection among children of St.-Petersburg, Russia at present

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The aim of our work was studied the prevalence *H. pylori* infection among children of St.-Petersburg in the years 2007-2018.

**Methods**: The screening of 1969 children and teenagers aged from 0 to 19 years of *H. pylori* infection was carried out (961 people in 2007-2011 and 1008 people in 2012-2018). Individuals without clinical manifestations of *Helicobacter pylori* infection living in Saint Petersburg were examined. IgG screening for *H. pylori* and Cag A *H. pylori* antibodies was performed using ELISA method with test-system produced DRG (Germany), Biohit (Finland).

**Results**: The results of the screening showed that as a whole 39.54 ± 1.6% examined children and adolescents possessed antibodies for bacterial *H. pylori* antigen in the years 2007-2011. At that antibodies for toxin-associated protein Cag A *H. pylori* were discovered in the screening of 37.77 ± 1.6% of the examined children and adolescents during those years. In 2012-2018, the screening results showed that as a whole 19.54 ± 1.2% examined children and adolescents had antibodies for bacterial *H. pylori* antigen. Antibodies for toxin-associated protein Cag A *H. pylori* were detected in the screening of 17.76 ± 1.2% of the examined persons.

**Conclusions**: Contemporary epidemic situation regarding *H. pylori* infection can be characterized by evidence of the infection rate decrease among young generations, in other words, the conducted study showed signs of so-called “cohort effect” that have been observed in some countries in Western Europe, North America, Japan. Further consideration of these peculiarities of the contemporary epidemic situation is necessary.

A.V. Svarval: None.

## P4.22 | Non-*Helicobacter pylori* Helicobacters were found to be closely related to *Helicobacter pylori*-negative or post-eradication human gastric diseases in Japan

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In Japan, the *Helicobacter pylori*(Hp)eradication regimen has been covered by the public health insurance system from 2013 in Hp positive chronic gastritis patients as well as gastroduodenal ulcer patients from 2000 and gastric MALT lymphoma, idiopathic thrombocytopenic purpura and endoscopically treated early gastric cancer patients from 2009. Since then, about ten million Hp positive cases have undergone the eradication therapy. In this post-*Hp* eradication era, the prevalence of non-*Hp*-Helicobacters (NHPH) including *Helicobacter suis* (Hs), *Helicobacter heilmannii sensu stricto* (Hhss) has attracted attention. We have collected endoscopically obtained samples from 248 Hp-negative patients and performed the PCR analysis. As a result, 47 cases (18.6%) were positive to NHPH. Among them 17 cases were positive to Hs, 9 cases were positive to Hhss and others could not be identified. The differences of regional distribution within Japan, gender and job could not show any statistic significances. As to the diseases, about half of the nodular gastritis cases, 20% of either MALT lymphoma or chronic gastritis cases were positive to NHPH. As to the duodenal follicular lymphoma no positive cases were found. Among the five post-Hp eradication chronic gastritis cases, three cases were positive to NHPH, including two Hhss positive cases. In conclusion, about 20% of the Hp negative gastric diseases were found to be related to NHPH. In the post-Hp eradication chronic gastritis cases, more than half cases were related to NHPH, suggesting the necessity of the precise scrutiny even after the Hp eradication.

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## P4.23 | Consent of doctors to follow the maastricht consensus report

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We assessed the commitment of doctors to follow the recommendations of the Maastricht Consensus Report. It was conducted an anonymous survey among 211 internists (n = 154) and gastroenterologists (n = 57), working in outpatient departments in different cities of Russia. The level of agreement was expressed by the degree: 0-I don't know, 1-disagree, 2-not fully agree and 3-fully agree.

**Results**: The doctors agreed to diagnose and eradicate HP in case of peptic ulcer in exacerbation (94.8%), in close relatives with stomach cancer (85.3%), in case of chronic atrophic gastritis (81.5%), as well as in long-term intake of PPI in 38.9% cases, NSAID in 42.6% cases, and functional dyspepsia in 41.2% of cases. Disagreement was significantly essential among therapists with experience up to 20 years without any categories ($X^2$ = 10.9537, $P \leq 0.05$, $X^2$ = 15.2542, $P \leq 0.05$). Doctors preferred using histobacterioscopy of gastrobioptat for diagnosis of HP both initially and as a control test after treatment (80.6% and 67.8%). Doctors were less willing to use the respiratory test and stool test (65.4% and 62.6% before, 61.1% and 58.3% after treatment). Among treatment regimens, doctors follow the standard triple therapy with Kla (90.05%), and even more to add bismuth to this therapy (99.5%). Doctors agreed to prescribe eradication therapy for 14 days (94.3%) than for 7 days (29.4%). Among the reasons for non-compliance the respondents noted low persistence of patients (93.4%) and limited diagnostic facilities (85.3%).

**Conclusion**: Inadequate agreement of therapists to recommendations may underlie the inefficiency of HP diagnosis and treatment.

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## P4.24 | Estimating 24-hour sodium excretion from spot urine in the Chilean arm of the Epidemiological iNvestigatIon of Gastric MAlignancy (ENIGMA) study

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**Background**: The first ENIGMA study was completed in low- (Antofagasta) and high-risk (Valdivia) areas of gastric cancer (GC) in Chile, with the aim to estimate the age-specific prevalence of *Helicobacter pylori* (*H. pylori)* infection while investigating other host/environmental factors associated with differences in GC risk. Using spot urine samples as an objective measure of salt intake in the two areas, we estimated 24-hour urinary sodium (Na) and potassium (K) excretion derived from several prediction equations.

**Methods**: Spot urine samples from 1287 individuals (1-69y) in Valdivia and Antofagasta were analysed for Na, K, and creatinine concentrations (Cobas, Roche Diagnostics). They were subsequently

used in several predictive equations to estimate individual 24-hour urinary excretions. Population estimates of 24-hour Na and K excretion included 1047 subjects after excluding those with missing height, weight, or age (n = 15), <15y (n = 225), and with Na concentrations above upper limits of linearity (n = 39).

**Results**: Mean 24-hour Na excretion based on the Tanaka equation was chosen as most comparable to the previous reports involving Chilean populations. Overall mean (SD) daily Na excretion for ENIGMA Chile was 3821 (908) mg/d. Na excretion and Na/K ratio were significantly higher in women from Antofagasta compared to Valdivia (3932 mg/d, 2.21 and 3618 mg/d, 1.97, respectively, both $P < 0.001$) while there was no significant difference observed in men.

**Conclusions**: Our finding that 24-hour Na excretion, reflecting Na intake, may be higher in women from a lower GC risk area merits further investigation. Additional analyses are underway stratifying by *H. pylori* seropositivity and gastric atrophy status.

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## P4.25 | Trends in the Prevalence of *Helicobacter pylori* (*H pylori*) infection - A seroprevalence study among symptomatic adults in Dhaka, Bangladesh

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**Background**: Bangladesh is a developing nation where reported H Pylori seroprevalence rates were >90% in late 1990's and 70% in 2013 seen among asymptomatic individuals. The Present study was aimed to know the H pylori seroprevalence among a cross section of symptomatic individuals at Dhaka hospital in Bangladesh.

**Methods**: This is a retrospective observational study conducted by using data collected from H pylori serology registry of Lab Aid Hospital - A tertiary Care Hospital at Dhaka. In the data registry patients' age, gender and other than abdominal pain no other clinical details were available. The test was done by a Chemiluminescent immunoassay (CLIA) kit – "Diasorin LIAISON" which quantitatively measures IgG antibodies to H pylori on the serum samples collected during October 2016 and April 2018. Data from 4009 subjects were available for analysis.

**Results**: Of the total 4009 subjects 2133 (56%) & 1876 (44%) were male and female respectively. The overall seroprevalence rates of H pylori infection were 52.48% (2104/4009). Comparatively higher seroprevalence rates were found among males (55.18%) and 21 to 60 years age groups of subjects (> 55%). Significantly lower seroprevalence rates were seen below 20 years (42%) and above 80 years (32%) group of subjects respectively.

**Conclusion**: The overall H pylori seroprevalence rates were 52.48% among these symptomatic subjects. Significant increasing in H pylori eradication therapy and PPI use especially by the symptomatic individuals along with an improvement of living and personal hygienic conditions may be responsible for this lower infection rate.

M. Ahmad: None.

## P4.26 | The prevalence of *Helicobacter pylori* Infection among pregnant women in south of Libya

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**Background**: *Helicobacter pylori* still one of the most frequent gastric pathogen in developing countries. The prevalence of *H. pylori* infection in pregnant women varies according to geographic area, socioeconomic conditions and method used to detect *H. pylori* infection. There is a lack of information about the seroprevalence of anti-*H. pylori* antibodies in pregnant women in Libyan south.

**Aims**: To determine the prevalence of the *H. pylori* infection in pregnant women. To correlate with the risk factors associated with *H. pylori* seropositivity in south region of Libya.

**Materials & Methods**: A Blood sample from (100) pregnant women and from (100) non- pregnant women (mean age 25 years), attending Sebha Hospital clinics, anti-*H. pylori* IgG seroprevalence were determined with ELISA method (Biotech USA), questionnaire covering Sociodemographic variables were completed by interview.

**Results**: The overall prevalence of *H. pylori* was (49%), but varied from (41%), in pregnant women to 57% in non- pregnant women, there was a gradual increase with age.

**Conclusions**: In Sebha region, *H. pylori* detection in pregnant and non -pregnant women was high of aged 25-30 years, which might be related to the socioeconomic status, domestic crowding and the source of drinking water as a major risk factors for *H. pylori* infection. Also we confirm that as a non- invasive method, the serologic test such as (ELISA) is a useful technique to detect *H. pylori* infection. Because of the high prevalence of the *H. pylori* in Libya, Further research is needed to establish the potential role of *H. pylori* in gastric and extragastric pathologies.

H.M. Khalafulla: None. A.M.A. Shahlol: None. A. Nami: None.

## P4.27 | Prevalence of *Helicobacter pylori* infections among patients Prevalence of *Helicobacter pylori* infections among patients referred for endoscopy at Laquintinie and General Hospital of Douala, Cameroon

**B. Eyoum Bille**

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**Background**: *Helicobacter pylori* is a worldwide infection. However, very few data are actually available on *H. pylori* seroprevalence in the Camroon population.

**Methods**: We carried out a transversal study in a sample of persons who met the following criteria: older than 15 years old, presence in the medicine internal (Laquintinie Hospital and General) during the period of the study whatever the reason. *H. pylori* infection was identified serologically by using ELISA. Several factors were evaluated including serological status, demographic information, the reason of the presence in the unit, factors influencing *H. pylori* infection: socio-economic status, siblings, promiscuity, consumption of alcohol, use of tobacco. The presence of clinical symptoms, such as dyspepsia and abdominal pain, was determined.

**Results**: Of the 842 participants, 370 (43.94%) were males, while 472 (56.06%) were females, with male: female ratio of 1.28. The ages of the participants ranged from 15 to 90 years with a mean of 44 ± 17 years. The overall prevalence was 70.5% (594/842). All patients with upper abdominal pains and frequent burping were *H. pylori* seropositive. The prevalence was 73.8% (273/370) in males and 68% (321/472) in females (OR: 1.32; 95%CI: 0.99-1.79 $P = 0.68$) and decreased with decreasing age ($P < 0.001$).

**Conclusion**: The seroprevalence of the *H. pylori* infection appears to be comparable to the rate encountered in developing countries. Considering this high rate of the *H. pylori* infection, eradication of *H. pylori* should be commonly recommended when facing gastrointestinal pathologies potentially induced by *H. pylori*.

B. Eyoum Bille: None.

## P4.28 | Dynamics of peptic ulcers healing in Europeoids of the Far North

**V. V. Tsukanov**; E. V. Kasparov; A. V. Vasyutin; J. L. Tonkikh

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**Aim**: To study the dynamics of peptic ulcers course in Europeoids of the Far North and middle latitudes of Siberia.

**Materials and methods**: 214 patients with peptic ulcer were examined in Norilsk city (133 were men, 81 were women; mean age 34.8 ± 2.1 years) located at 69° of north latitude; and 179 patients with peptic ulcer disease in Krasnoyarsk city (115 men, 64 women; mean age 42.5 ± 1.9 years), located at 56° north latitude. The distance between Krasnoyarsk and Norilsk is 1,500 km. All patients had *Helicobacter pylori* infection. Fibrogastroduodenoscopy was performed before the start of treatment and 14 days after the start of treatment.

**Results**: All patients received standard treatment, including proton pump inhibitors (PPIs) and *Helicobacter pylori* eradication. The effectiveness of *Helicobacter pylori* eradication schemes did not differ in Norilsk and Krasnoyarsk and was, respectively, 84% and 86%. The proportion of persons with a stomach ulcer was 25.1% in Krasnoyarsk and 31.5% in Norilsk ($P = 0.2$). The duration of epigastric pain was 15.8 ± 0.8 days in Norilsk and 8.6 ± 0.7 days in Krasnoyarsk ($P < 0.001$). After 14 days of treatment, ulcers healed in 92.2% of individuals in Krasnoyarsk and in 65.9% of patients in Norilsk ($P < 0.001$).

**Conclusion**: The healing of ulcers of the gastroduodenal zone was in Europeoids of the Far North much slower than in residents of middle latitudes.

V.V. Tsukanov: None. E.V. Kasparov: None. A.V. Vasyutin: None. J.L. Tonkikh: None.

## P4.29 | Prevalence of CagA *Helicobacter pylori* in schoolchildren of Buryatia

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**Aim**: To study the prevalence of CagA strain of *H. pylori* infection in Buryatia (Siberia, Russian Federation) schoolchildren in the territory with high frequency of stomach cancer.

**Materials and Methods**: We picked up by random 131 children out of 790 schoolchildren of Buryatia (31 Europeoids, 100 Buryat-Mongoloids among them) and performed CagA *H. pylori* verification in blood serum.

**Results**: CagA *H. pylori* in the examined schoolchildren of Buryatia accounted to 45.0%. In the age group from 7 to 11 years the share of infected children was 31.7%, and in the ages from 12 to 17 the presence of *H. pylori* CagA strain was found in 51.1% ($P > 0.05$). In girls the infection was marked in 48.8%, and in boys in 39.2% ($P > 0.05$). In children in ethnic groups the infection was verified in 42.0% of the Butyats and in 54.8% of the Europeoids ($P > 0.05$). In the Buryats in junior age group the presence of *H. pylori* CagA was determined in 29.6%, and in senior age group in 46.6% ($P > 0.05$). In the Europeoids the shares of the infected children accounted to 35.7% and 70.6 % correspondingly; $P = 0.05$.

**Conclusion**: *H. pylori* CagA infection in Buryatia schoolchildren accounted to 45.0%. The differences between the figures for the Mongoloids and Europeoids have not been found. The contamination with the said infection mainly happens in the ages earlier than 12 years. In older ages the share of infected schoolchildren tends to grow. In the Europeoids this index is meaningful.

V.A. Vshivkov: None. T.V. Polivanova: None. V.V. Tsukanov: None.

## P4.30 | *Helicobacter pylori* in patients with coeliac compared to healthy blood donors

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**Background**: Studies suggest that *Helicobacter pylori* (Hp) infection and Coeliac disease (CD) might be inversely related. Hp infection may start in the ages of 0-10 years thereafter the increase in carriage is slow. Our aim was to examine possible association between *H. pylori* (± cagA) and CD.

**Materials & Methods**: CD-Sera (stored −20°C) from patients with proven CD (N = 175; Age ≥ 18) sampled prior to CD diagnosis. Controls=blood donors (BD) sera (N = 153). Analysis was done on Liasion XL (Diasorin, Italy; anti-Hp IgG). Borderline and positive sera were analysed for IgG anti-cagA (Genesis Diagnostics, Littleford, Cambridgeshire, UK).

**Results & Comments**: The carriage rate in BD was 6.5%. CD patients were positive in 10.9% in addition 8.6% had borderline levels of Hp specific IgG antibodies. Anti-cagA IgG was detected in 4 out of 10 BD and in 4 of 18 CD. Mean age (*M*) in CD patients status (Hp+/cagA-): 39.4 years; status (Hp+/cagA+): (*M*) 60.5 years. Among BD status (Hp+/cagA+): (*M*) 45.3 years (Table 1).

As CD is an "allergic" disease with known stimulus, it is tempting to speculate that presence of Hp preferably harbouring cagA+ (or similar antigens) might result in an immune response that possibly may delay onset of CD in disposed individuals.

**TABLE 1.** Antibody presence in Healthy Blood Donors and Patients suffering from Coeliaci

| | | Clinical Status | | | | | |
|---|---|---|---|---|---|---|---|
| | | Blood donors (N = 153) | | | Untreated coeliac patients (N = 175) | | |
| | | Mean age | | | Mean age | | |
| HP status | | N | % | Total | N | % | Total |
| Positive | | 10 | 6.5 | | 18 | 10.3 | |
| | *CagA +* | 4 | ND | 45.3 | 4 | | 60.3 |
| | *CagA −* | 6 | ND | ND | 14 | | 39.4 |
| Borderline | | 0 | 0 | | 15 | 8.6 | |
| | *CagA +* | *ND* | | | 0 | | |
| | *CagA −* | *ND* | | | 15 | | |
| Negative | | 143 | 93.5 | | 142 | 81.1 | |

K.K. Melby: None. L.S.H. Nissen-Meyer: None. K.E.A. Lundin: None.

## P4.31 | Prevalence of *Helicobacter pylori* infection in dynamic (2008-2016) in Saint-Petersburg, Russia

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**Background**: It is still important to estimate prevalence of *H. pylori* in different population for monitoring of infection frequency, check the results of mass eradication therapy and prognosis of risk of stomach cancer. The aim: to estimate frequency of *H. pylori* infection in patients with dyspepsia by breath ammonium test in St-Petersburg, Russia.

**Methods**: 221 patients with dyspepsia were observed: 134 patients in 2008-2009, 37 patients in 2012-2013, 50 patients in 2015-2016. Detection of *H. pylori* was made by non-invasive breath ammonium test (HELIC ABT, Association of Medicine and Analytic, St-Petersburg). The process of diagnostic: 1. Detection of basal level of ammonium in oral cavity; 2. Drinking of carbamide solution: 0.5 g of carbamide in 50 mL of still water; 3. Hydrolysis of carbamide by urease of *H. pylori*: $(NH_2)_2CO + H_2O \leftrightarrow 2NH_3\uparrow + CO_2\uparrow$; 4. Detection of loading level of ammonium in oral cavity.

**Results**: Results in 2008-2009 frequency of *H. pylori* infection in patients with dyspepsia was 78%, in 2012-2013 - 56%, in 2015-2016 - 45% ($P < 0.05$). It is similar with results of differ Russian studies (38.5%-43.0%) (R. Plavnik, V. Nevmerzhitskiy, I. Voinovan, D. Bordin et al., 2018; N.V. Bakulina, V.I. Simanenkov, I.G. Bakulin, T.A. Ilchishina, 2018).

**Conclusion**: We can see a progressive decreasing of frequency of *H. pylori* infection in patients with dyspepsia in St-Petersburg, Russia. It can be associated with widely administered eradication therapy. Also this fact can be a promising for decreasing of frequency a stomach cancer in future in our region.

N.V. Baryshnikova: None. Y.P. UsPenskiy: None. A.A. Gnutov: None. M.A. Dmitrienko: None.

## POSTER ROUND 4.2 PAEDIATRICS

### P4.32 | Genetic predisposition to innate mannose-binding lectin and L-ficolin deficiencies are associated with a higher risk of *cagA* positive chronic *Helicobacter pylori* infection in adolescents

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Currently, only a few molecules are known to activate the lectin pathway of complement activation: the human ficolins and the mannose-binding lectin (MBL). It has been shown that the *MBL2* gene polymorphisms are associated with a risk of developing more severe gastric mucosal atrophy in *Helicobacter pylori(Hp)*-infected patients and gastric cancer risk. The influence of the *MBL2* and *FNC2* genes variants on the c*agA* positive *Hp* infection rate are not studied well.

**Methods**: 93 Caucasians adolescents (aged 12-17, Krasnoyarsk, Siberia, Russia), were tested for anti-*Hp-cagA* antibodies in plasma. As additional population control, we used 203 specimens of dried blood spots of newborns from Krasnoyarsk. Genotyping was carried out using the RFLP approach. Four polymorphisms were studied: rs11800451 (*MBL2*), rs1800450 (*MBL2*), rs17549193 (*FCN2*), and rs7851696 (*FCN2*). Two-tailed Fisher test was used.

**Results**: Carriage of the rare allele in the polymorphic region rs1800450 of the *MBL2* gene and the homozygous state of the rare allele T of polymorphism rs17549193 of the *FCN2* gene are associated with an increased risk of *cagA* seropositivity (OR = 2.36 (1.03-5.4), *P* = 0.04 and OR = 5.69 (1.08-29.99), *P* = 0.04, respectively). Newborns group had an intermediate genotypes prevalence.

**Conclusion**: We suggest that the innate MBL and L-ficolin deficiencies are associated with a higher risk of *cagA* positive *Helicobacter pylori* chronic infection in adolescents. It may be because of alterations in lectin-mediated activation of complement and opsonization which is especially characteristic for *CagA* positive strains of bacteria. Study was funded by Krasnoyarsk Region Science and Technology Support Fund.

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### P4.33 | Production of reactive oxygen species in culture of blood monocytes in children with peptic ulcers associated with *Helicobacter pylori*

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**Aim**: To determine reactive oxygen species (ROS) in culture of blood monocytes in children with peptic ulcers associated with *Helicobacter pylori*.

**Methods**: 44 children (23 boys, 21 girls, average age 14.2 years) with *Helicobacter pylori*-associated ulcers of the gastroduodenal zone (group A) and 34 children (18 boys, 16 girls, average age 13.9 years) with *Helicobacter pylori* infection, but without peptic ulcers (group B) were examined. *Helicobacter pylori* was determined by the C-13 urea breath test in all children. Culture of blood monocytes isolated by separation on ficoll and adhesion on plastics. The baseline level and the level after zymosan stimulation of the ROS in the culture of blood monocytes were determined by the chemiluminescent method.

**Results**: We found a sevenfold increase in the baseline production of ROS in the culture of blood monocytes in group A compared with group B ($P = 0.007$). After monocyte activation by zymosan, the level of ROS was 3.5 times higher in group A compared with group B ($P < 0.001$).

**Conclusions**: The processes of phagocytosis in the blood are more active in children with peptic ulcers of the gastroduodenal zone in comparison with children without peptic ulcers.

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### P4.34 | Prevalence of gastric Non-*Helicobacter pylori* Helicobacters in Mexican children with gastroduodenal manifestations

**C. Romo-González**[1]; L. Morelia-Mandujano[1]; D. León-Cortes[1]; M. Camorlinga-Ponce[2]; A. Smet[3]; C. De Witte[4]; F. Haesebrouck[4]; R. Coria-Jimenez[1]; E. Montijo-Barrios[5]

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**Background**: Non-*Helicobacter pylori* Helicobacters (NHPH) have been described in patients with gastroduodenal diseases. Their

prevalence has been reported between 0.2- 12% in adults or up to 32.7% in children. In Mexico, the prevalence is practically non-existent. Aim: This study aimed at estimating the prevalence of gastric NHPH and a possible co-infection with *H. pylori* (Hp) in children with gastroduodenal manifestations (GM).

**Methods**: We obtained biopsies of antrum (A), body (B) and incisure (I) from 30 children with GM attended at National Institute of Pediatrics in Mexico City. DNA was extracted from the biopsies and detection of NHPH was performed by PCR. The presence of Hp was evaluated by culture and PCR.

**Results**: The prevalence of NHPH was 33.3% (10/30). Of the ten patients, five had co-infection between *H. suis* and *H.bizzozeronii*; three had only *H. bizzozeronii* and two *H. felis*. *H. heilmannii* was not found in any patient. The prevalence and colonization pattern was as follows: *H. suis* 16.6% (5/30), colonization in A, B and I of all these patients; *H. felis* 13.3% (4/30), 2 (AB, AI); 1(B), and 1(I); *H. bizzozeronii* 26.6% (8/30) consisting of 5 (ABI); 1(AI); 1(B), and 1(I). Hp was found in 30% (9/30), a mixed infection with Hp and *H. felis* was present in two patients.

**Conclusions**: The prevalence of NHPH was 33.3%. There was co-infection between *H. suis* and *H. bizzozeronii*, and Hp and *H. felis*. Besides, these species can be found in any of the three regions - antrum, body or incisure.

C. Romo-González: None. L. Morelia-Mandujano: None. D. León-Cortes: None. M. Camorlinga-Ponce: None. A. Smet: None. C. De Witte: None. F. Haesebrouck: None. R. Coria-Jimenez: None. E. Montijo-Barrios: None.

## P4.35 | Changes in the prevalence of reflux oesophagitis and *Helicobacter pylori* infection in symptomatic children

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**Introduction**: The relationship between *Helicobacter pylori* (H pylori) infection and reflux oesophagitis (RE) remains a matter of controversy, particularly in children. The prevalence of H pylori infection in children has been steadily declining over the last decade, meanwhile the incidence of gastroesophageal reflux disease has increased. Aim: To assess the changes in the relationship between H pylori infection and RE among gastroscopied symptomatic children, in our unit.

**Methods**: This was a retrospective single center study of all esophagogastroduodenoscopies performed in consecutive symptomatic children. Two study lots were compared, the first one comprised between 2001-2010 (1142 children, 710 girls) and the second between 2015-2017 (666 children, 414 girls). Active H pylori infection was proved by rapid urease test and histological examination. The RE was graded according to Hetzel-Dent classification, where the grade 2 was considered as erosive esophagitis.

**Results**: The active H pylori infection was documented in a higher proportion in the second studied group (65.31%) compared to the first study group (53.06%). On the contrary, the global prevalence of the RE was higher in the first studied lot (55.60%) compared to the second one (44.59%), and where erosive reflux oesophagitis was predominant (64.88%). The prevalence of RE in relation to the presence of H pylori infection was higher in infected children in both studied groups (77.06% vs 66.66%).

**Conclusion**: The recent decline of H pylori infection observed in developed countries is not evident in our study. Unlike other studies, our research showed that H pylori infection was positively associated with RE.

V. Hurduc: None. L. Bordei: None. A. Zamfirescu: None.

## P4.36 | Changes of urine *H. pylori* antibody test at 2-year interval in junior high school students in Japan

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**Objectives**: *H. pylori* infection occurs mainly in childhood, but the dynamics of its infection in this period have not been clarified. The aim of this study was to examine the change of *H. pylori* status in junior high school students using urine antibody test.

**Subjects and Methods**: Subjects were 986 junior high school students attending five schools in Tambasasayama-city and submitted urine samples at two-year intervals. Urine antibody test was performed using URINELISA kit and antibody titer of ≥1.0 and <1.0 were judged to be positive and negative, respectively. Students with positive results were asked to undergo urea breath test (UBT).

**Results**: 906 and 40 students showed persistently negative and positive results of urine antibody, respectively. Twelve students with negative tests turned positive, while 28 with positive tests turned negative. Three students had received *H. pylori* treatment among those whose results turned negative. Twenty-six students with positive results underwent UBT. Six of the 12 students who turned positive underwent UBT, but all showed negative results. Of the 40 students who remained positive, 18 underwent UBT with positive results in 10 students.

**Conclusion**: Urine antibody test is convenient for screening but caution is required for low positive predictive value. In this study, some students turned positive in urine antibody test but no new infection was proven. Our results suggest that new infections in junior high school students are rare in Japan.

M. Okuda: None. M. Konishi: None. R. Miyamoto: None. Y. Lin: None. S. Kikuchi: None. Y. Takeshima: None.

## P4.37 | *Helicobacter pylori* infection and childhood overweight/Obesity

**M. Kori**[1]; O. Pundack[2]; C. Topf Olivestone[1]; L. Hofi[1]

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**Objective and study**: The reduction in prevalence of *Helicobacter pylori* (*HP*) infection coincides with the increase in the incidence of obesity, and might be a contributing factor. We aimed to evaluate the association between *HP* infection and childhood overweight and obesity.

**Methods**: Patients diagnosed between 1/2013 and 8/2018 with *HP* infection by endoscopy with positive culture were included. For each *HP* positive patient, a *HP* negative, age and gender matched control was identified. Data included; age, gender, height, weight, BMI, BMI percentile and indication for endoscopy. Children with missing anthropometric data or diagnosed with diseases that might affect growth were excluded (Celiac, Crohn's Disease etc.).

**Results**: 145 *HP* positive and 145 age and gender matched negative controls were included. 64.1% (186/290) female, mean age 13.2 ± 3.61. Overweight (BMI between the 85th-95th percentile) and obesity (BMI > 95th percentile) were present in 51/290 (17.6%) of children. Among the *HP* positive children, 9.7% were overweight and 7.6% obese. Among the *HP* negative children, 9.0% were overweight and 9.0% obese, demonstrating no differences between the groups. The main indication for endoscopy was abdominal / epigastric pain (223/290) 76.9%, other indications included vomiting, anemia, dysphagia and others. There was no difference in the BMI percentile by indications for endoscopy. The percent of children with a BMI ≥ 85% did not differ by gender and was similar in all age groups.

**Conclusions**: No association between *HP* infection and childhood overweight or obesity was demonstrated. This is in contrast to previous pediatric studies demonstrating an inverse correlation.

M. Kori: None. O. Pundack: None. C. Topf Olivestone: None. L. Hofi: None.

## P4.38 | Characteristics of gastroduodenal pathology in children in families of parents with peptic ulcer disease

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**Introduction**: Genetic aspects of the peptic ulcer disease pathogenesis (PUD) have long been known (Miftahussurur M. & Yamaoka Y., 2015), but in real clinical practice, the family approach is little used to treat children and adults.

**Aim**: To study the prevalence and clinical features of gastroduodenal pathology in children in families of parents with PUD.

**Methods**: Clinical screening of gastroduodenal pathology was carried out by a single-step method in rural areas and performed by a continuous method in 295 Caucasoids children (137 boys and 158 girls) of school age and in 571 adults (258 men and 313 women) from the number of their parents. Esophagogastroduodenoscopy was performed on 40% of a random sample in 241 adults (105 men and 136 women) and in 121 children (62 boys and 59 girls). The determination of *Helicobacter pylori* IgG was performed in 504 adults and in 265 children using the serological method.

**Results**: *Helicobacter pylori* IgG was found in 70.6% of children. The prevalence of ulcerative and erosive defects of the gastroduodenal zone in children was 13.5%. The prevalence of PUD in adult patients was 11.2%. The frequency of *Helicobacter pylori* ($P$ = 0.03), ulcerative and erosive defects of the gastroduodenal mucosa ($P$ = 0.009) was higher in children of parents with PUD, compared with children from families where the parents had no PUD.

**Conclusion**: We found a pronounced association of the gastroduodenal mucosa ulcerative and erosive defects frequency and *Helicobacter pylori* infection indicators in children with the presence of PUD in their parents.

V.V. Tsukanov: None. A.V. Vasyutin: None. J.L. Tonkikh: None.

## P4.39 | *Helicobacter pylori* in school children predisposed to ulcer disease

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**Aim of the research**: To study *Helicobacter pylori* frequency in children with family predisposition to ulcer disease.

**Material and Methods**: 80 Europoid children and 83 Evenk Mongioid children with gastroenterologic complains were picked up by random in Evenkia (Extreme North, Siberia, Russia) in the ages from 7 to 17 years. Age-gender structure in both cohorts was identical. We performed gastroscopy with biopsy sampling from stomach antrum mucosa. *Helicobacter pylori* identification was carried out by morphological method after Giemsa coloring. The analysis of statistical meaning of qualitative characteristics was made by $\chi^2$ criterion under <0.05.

**Results**: Pylori frequency in Europoid children in the families of the parents with ulcer disease in comparison with the subjects without family predisposition amounted to 92.6% and 67.9% accordingly (=0.0136). In the Evenk population characterized by heavy family medical history related to ulcer disease there wasn't found any

considerable increase of. ylori prevalence in children in comparison with the children without family predisposition (in 93.8% and 84.4% correspondingly).

**Conclusion**: In Evenkia we have marked extremely frequent *H. pylori*. In Europoid children we found the association between infection prevalence and diagnosed ulcer disease in the family members. In the Evenks such associations haven't been revealed. The said results are indirect proof of high family transmission of the microorganism in the Extreme North inhabitants.

T.V. Polivanova: None. V.V. Tsukanov: None. V.A. Vshivkov: None.

## P4.40 | Features of gastroduodenal pathology in children in families of parents with uninvestigated dyspepsia

**V. V. Tsukanov**; A. V. Vasyutin; J. L. Tonkikh

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**Introduction**: It is known that one of the main path of *Helicobacter pylori* (*H. pylori*) infection is family transmission (Sjomina O. et al., 2018). But the number of works on the association of pathology in children and parents is insignificant.

**Methods**: Screening of gastroduodenal pathology was performed by a single-step method in 295 Caucasoids school age children and 571 adults from the number of their parents in the countryside. The average age was 12.4 years in children and 39.9 years in adults. Dyspepsia was diagnosed according to Rome III criteria (Tack J. et al., 2006). Esophagogastroduodenoscopy was performed among 121 children in 40% of the random sample. *H. pylori* was determined by a serological method in 265 children.

**Results**: Uninvestigated dyspepsia was detected in 25.2% of parents (23.6% in men, 26.2% in women). The frequency of dyspepsia in children in families of parents with dyspepsia was 40.5%, and in children in families of healthy parents - 9.0% ($P < 0.001$). Erosions and ulcers in the gastroduodenal zone were registered in 14.7% children of parents with dyspepsia and in 3.8% children of healthy parents ($P = 0.09$). *H. pylori* IgG was determined in 69.8% of children with dyspepsia and in 51.7% of children without dyspepsia ($P = 0.02$).

**Conclusion**: We found an association of the prevalence of dyspepsia, gastroduodenal mucosa ulcerative and erosive defects in children with dyspepsia in their parents. In children with dyspepsia, there was also a clear connection with the prevalence of the frequency of *Helicobacter pylori* in comparison with persons without dyspepsia.

V.V. Tsukanov: None. A.V. Vasyutin: None. J.L. Tonkikh: None.

## P4.41 | The interrelation of *H. pylori* infectivity with the persistence of diareegenic *E.coli* in children with chronic gastritis and associated atopic diseases

A. P. Listopadova[1]; V. P. Novikova[1]; E. A. Orishak[2]; L. Y. Nilova[2]; **N. V. Baryshnikova**[3,4]; Y. P. Uspenskiy[3,1]

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**Background**: The influence of *H. pylori* (HP) on the state of intestinal microbiota and the incidence of atopic diseases are contradictory.

**The aim**: To identify the relationship between HP and persistent diarrhegenic E.coli in children with chronic gastritis (CG) and atopic diseases.

**Methods**: 48 patients with CG (9 to 18 years) were divided into groups: with CG - n = 22; with CG + atopic dermatitis (ATD) - n = 19; with CG + bronchial asthma (BA) - n = 7. All were serotyped strains of E. coli with typical properties. Identify specific genomic sequence ETEC, EPEC, EHEC, and EIEC EAgEC by PCR.

**Results**: In patients with CG + BA, HP is significantly more frequent than CG + ATD and CG (77.27%, 68.42% and 100%, p1,3 < 0.01 and p2,3 < 0.01). In 48 children, 11 E. coli isolates (23.9%) were isolated. In patients with BA and CG diarrheal E. coli was not detected. But in patients with AD and CG, 5 strains were isolated, and with CG - 6 strains with virulence genes: DAEC -1 strain, EAggEC - 6, EPEC and ATEC - 3 strains. One isolate - defined as EHEC. Correlation between the presence of diarrheal E. coli. and HP have all surveyed not revealed.

**Conclusion**: In children with CG + BA HP infection was detected more often than in patients with CG + ATD and with CHS. Diarrhegenic E.coli with CG + BA was not detected. The presence of diarrheal E. coli did not depend on the persistence of HP in the gastric mucosa.

A.P. Listopadova: None. V.P. Novikova: None. E.A. Orishak: None. L.Y. Nilova: None. N.V. Baryshnikova: None. Y.P. Uspenskiy: None.

## P4.42 | Destruction of stomach and duodenum mucosa in two age groups of *Helicobacter pylori* children

V. A. Vshivkov; T. V. Polivanova; **V. V. Tsukanov**

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**Aim of the research**: To study the frequency and character of the process in stomach and duodenum mucosa in *H. pylori* children.

**Material and methods**: We have examined 338 schoolchildren of Siberia (Russian Federation) with gastroenterological complains in the ages from 7 to 17 years (98 subjects of 7-11 years and 240 of 12-17 years). We performed gastroscopy with biopsy of antrum. *H. pylori* was identified by histology for stomach bioptats after Gimza coloring. Analysis of statistical meaning of the differences between qualitative characteristics was carried out by $\chi^2$ criterion under <0.05.

Results: Children in the ages from 7 to 11 years are infected in 42.9% and in the ages from 12 to 17 years in 63.8% ($P$ = 0.0004). In the children of earlier ages with bacterial invasion and non-infected children ulcer disease was diagnosed in 2.4% and 1.8% ($P$ = 0.8366) subjects, erosive gastritis in 11.9% and 3.6% ($P$ = 0.1129), erosive duodenitis 7.1% and 0% ($P$ = 0.0422) accordingly. Among the elder children with *H. pylori* bacterial invasion and without it ulcer disease was diagnosed in 2.0% and 3.4% (=0.4779), erosive gastritis in 8.5% and 14.9% ($P$ = 0.1225), erosive duodenitis in 6.5% and 4.6% cases ($P$ = 0.5379) accordingly.

Conclusion: Pathogenic aspect of *H. pylori* influence on the development of destructive process in stomach and duodenum mucosa in children is not evident, except for junior children. In them, in *H. pylori* invasion erosive duodenitis is more frequent.

V.A. Vshivkov: B. Research Grant (principal investigator, collaborator or consultant and pending grants as well as grants already received); Modest; The present research was made under the support of Krasnoyarsk Regional Fund of Science according to the research project «The role of genetically determined factors of pathogenicity related to Helico. T.V. Polivanova: A. Employment (full or part-time); Modest; The present research was made under the support of Krasnoyarsk Regional Fund of Science according to the research project «The role of genetically determined factors of pathogenicity related to Helico. V.V. Tsukanov: None.

## POSTER ROUND 5.1 GASTRIC CANCER AND CANCEROGENESIS

### P5.01 | Effect of *Helicobacter pylori* and microsatellite state on the metachronous recurrence of gastric epithelial neoplasia

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**Background/Aims**: It has been known that *Helicobacter pylori* eradication could prevent the metachronous recurrence after endoscopic treatment of gastric epithelial neoplasias. It was unlikely that *H. pylori* eradication therapy gave a chance of complete prevention of gastric cancer. The aim of this study was to determine the long term results and clinical outcomes according to *H. pylori* infection and microsatellite state.

**Method**: We designed the retrospective cohort study with the patients treated by endoscopic mucosal resection / submucosal dissection since 1999, and diagnosed as gastric epithelial neoplasias. During long term follow up periods (4 to 14 years), we checked the disease recurrence regularly, and all tissues were examined at the 7 sets of microsatellite loci linked to the tumor suppressor gene locus initially. When *H. pylori* infection was identified, all patients had eradication therapy.

**Results**: A total of 120 patients were enrolled and divided into three groups - *H. pylori*-negative and microsatellite stable (MSS)/ *H. pylori*-positive and MSS / microsatellite instability (MSI). After *H. pylori* eradication, there were significant differences of rate of metachronous recurrence and surgical intervention in MSI group, compared with MSS group (2.8% vs 10.3%, $P$ < 0.01) (4.9% vs 17.9%, $P$ = 0.02). It was noteworthy that there were no recurrences in *H. pylori*-positive with MSS after successful eradication.

**Conclusion**: The beneficial effect of gastric cancer prevention by *H. pylori* eradication could be accomplished in MSS state. In patients with gastric epithelial neoplasias with MSI state, meticulous long-term follow up program should be necessary for the detection of metachronous recurrence.

H. Ahn: None. Y. Kim: None. J. Kim: None. W. Chung: None.

### P5.02 | Putative impact of CagA protein on DNA damage repair modulation during *Helicobacter pylori* infection

**E. Kontizas**[1,2]; S. Tastsoglou[3]; T. Karamitros[1]; Y. Karayiannis[1,2]; P. Kollia[2]; A. Hatzigeorgiou[3]; A. Mentis[1]; D. N. Sgouras[1]

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*Helicobacter pylori* (*Hp*) infection establishes chronic inflammation which promotes genomic instability by inducing conditions of oxidative and replication stress and a plethora of DNA damages. The occurring DNA damages of gastric epithelial cells require activation of DNA damage repair (DDR) mechanisms, which have been reported to be modulated by the infection. *Hp* CagA protein interferes with host cell functions such as proliferation, apoptosis and chromosomal integrity. Its pathogenic activity is partly regulated by hierarchic tyrosine phosphorylation on repeated EPIYA-motifs, by host kinases. Our aim was to identify putative effects of *Hp* infection and CagA on DDR-mechanisms, investigating the transcriptome profile of AGS cells, infected with wild-type, ΔCagA and EPIYA-phosphorylation-defective mutant strains. RNA-Seq was performed on polyA-selected transcripts and differentially expressed genes were visualized on KEGG-Pathway maps, for each DDR-mechanism. Key DDR-components that were observed to be deregulated

in a CagA-dependent manner were validated via Western blot. Transcriptome analysis revealed that a significant number of DDR-genes were downregulated during *Hp* infection such as APE1, MUTYH and FEN1 in Base-Excision-Repair, POLD1 in Nucleotide-Excision-Repair, MLH1 and MSH2 in Mismatch-Repair, RAD51 and RAD54 in Homologous-Recombination and POLM in Non-Homologous-End-Joining. RAD51, FEN1, LIG1, NTHL1 and MUTYH downregulation was observed to be CagA-related and these observations were verified on the protein expression level. APE1 protein was found to be overexpressed in CagA-dependent manner, denoting a potential negative feedback loop. Our study highlights the role of CagA, as major contributor of *Hp* infection-mediated DDR-modulation, rendering gastric cells vulnerable to genomic instability and thus potentially contributing to carcinogenesis.

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## P5.03 | Risk of progression of gastric intestinal metaplasia based on anatomic region affected

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**Introduction**: Gastric cancer (GC) is the second leading cause of cancer-related death in the world. Most gastric adenocarcinomas are preceded by a cascade of well-defined precursor lesions, including intestinal metaplasia (GIM) and dysplasia. We aimed to investigate the rates of progression of GIM to dysplasia and GC in a low incidence country based on area of stomach affected.

**Methods**: All patients with GIM detected at gastroscopy in Tallaght University Hospital from 2008 to 2012 were identified in the hospital database. Follow-up data were evaluated until 31st December 2018. I

**Results**: 268 patients were followed for GIM in the antrum alone and 8 of those progressed (3%), 5 to GC and 3 to dysplasia. 68 patients were followed for GIM isolated to the corpus and 3 of those progressed (4.5%), 1 to dysplasia and 2 to GC. 40 patients with GIM in antrum and corpus were followed and 1 developed GC (2.5%). 35 patients with cardia IM were followed and 1 developed GC (2.9%).

**Conclusion**: Although current guidelines for low-GC incidence countries are only to survey patients with GIM in antrum and corpus, patients followed with one area of GIM had a significant yield of progression.

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## P5.04 | Prognostic role of long non-coding RNA HOTAIR expression in gastric cancer and association with preneoplastic conditions and *H. pylori*

**V. Petkevicius**[1,2]; R. Steponaitiene[2]; C. Thon[3]; J. Skieceviciene[2]; P. Malfertheiner[3]; J. Kupcinskas[1,2]; A. Link[3]

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**Introduction**: HOTAIR is long non-coding RNAs that plays an important role in gene regulation and has been shown to be upregulated in various tumors, including gastric cancer (GC).

**Aims & Methods**: The aim of this study was to evaluate HOTAIR expression in GC and preneoplastic gastric conditions in relation to *H. pylori* status. HOTAIR expression was analyzed in tissue samples of 81 GC patient (paired samples from tumor and corresponding adjacent gastric mucosa) and biopsy samples from patients with atrophic gastritis (AG), chronic gastritis (NACG), and controls (total n = 88). Quantitative HOTAIR expression analysis was performed using SYBR Green assay. *H. pylori* was determined by serology, microbiology and histological evaluation.

**Results**: Paired GC samples analysis revealed higher positivity rate of HOTAIR in tumor tissue compared to adjacent gastric mucosa (65.4% vs 8.6%, $P < 0.001$). Tumor positivity for HOTAIR expression was associated with shorter overall survival in diffuse type GC patients compared to patients without detectable HOTAIR expression ($P = 0.006$). HOTAIR was undetectable in histologically confirmed normal gastric mucosa samples from control group and NACG. HOTAIR expression was found in 24% of patients with AG. The HOTAIR positivity was strongly related to intestinal metaplasia (52.4%) and expression was positively associated with the grade of intestinal metaplasia ($P < 0.001$). HOTAIR expression was determined in 20.8% of *H. pylori* positive samples and in 2.9% of *H. pylori* negative samples ($P = 0.017$).

**Conclusion**: HOTAIR expression increases in step-wise manner in correlation to progression of preneoplastic condition and is associated with worse prognosis in diffuse type of GC.

V. Petkevicius: None. R. Steponaitiene: None. C. Thon: None. J. Skieceviciene: None. P. Malfertheiner: None. J. Kupcinskas: None. A. Link: None.

## P5.05 | Clinical significance of reddish depressed lesions on development of metachronous gastric neoplasm in patients underwent endoscopic resection followed by *Helicobacter pylori* eradication

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**Background & aim**: Reddish depressed lesions (RDLs) frequently observed after *Helicobacter pylori* (HP) eradication. A few studies reported about RDLs in high-risk patients for gastric cancer after HP eradication. We assessed the clinical significance of the emergence of RDLs in the metachronous neoplasm after curative endoscopic resection (ER) of gastric neoplasm followed by HP eradication.

**Materials & Methods**: From January 2000 to April 2018, 1280 patients underwent ER for high grade dysplasia and early gastric cancer. 191 consecutive patients achieving successful HP eradication after curative ER were included. Patients were categorized into two groups: the metachronous group (n = 14) and the non-metachronous group (n = 171). The emergence of RDLs were assessed by white light imaging endoscopy after successful eradication. Other endoscopic findings including degree and scale of intestinal metaplasia, atrophic gastritis and xanthoma were also assessed.

**Results**: Mean follow up periods were 46.73 (± 2.110) and 68.86 (± 7.214) in each group. Baseline characteristics of both groups were similar except cigarette smoking (50% *vs* 22%, $P = 0.018$). Emergence of RDLs was 92% (13/14) in the metachronous group and 55% (97/177) in the non-metachronous group. The patients with emergence of RDLs was significantly more likely to develop metachronous cancer (14.0% vs 1.0%, $P < 0.001$). Positive predictive value and negative predictive value of emergence of RDLs for metachronous lesion were 1.02% and 86.02%.

**Conclusions**: Emergence of RDLs is useful endoscopic findings in the negative predictions of metachronous neoplasm development after curative ER for previous gastric neoplasm followed by HP eradication.

S. Kim: None. S. Hong: None. J. Lee: None.

## P5.06 | LATS2 controls gastric epithelial integrity by restricting epithelial-mesenchymal transition and intestinal metaplasia induced by *Helicobacter pylori* infection

S. Molina-Castro[1,2]; **C. Tiffon**[1]; J. Giraud[1]; H. Boeuf[3]; E. Sifre[1]; A. Giese[1]; G. Belleannée[4]; P. Lehours[1,4]; E. Bessède[1,4]; F. Mégraud[1,4]; P. Dubus[1,4]; C. Staedel[5]; C. Varon[1]

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**Background & Aims**: Gastric carcinoma is mostly related to infection with *Helicobacter pylori*, which disrupts the gastric mucosa turnover and elicits an epithelial-mesenchymal transition (EMT) and preneoplastic trans-differentiation. The Hippo pathway controls stem cell homeostasis; its core is constituted by the tumor suppressor kinase, LATS2, which negatively regulates the oncogenic co-transcription factors YAP1. This pathway was investigated in this context of infection.

**Methods**: Gastric epithelial cell lines (AGS and MKN74) and non-gastric non-cancerous epithelial cell lines (HMLE and RPE1) were challenged by *H. pylori* to investigate the regulation of the Hippo pathway. LATS2 was silenced using small interfering RNAs. The expression of Hippo pathway related genes, EMT and intestinal metaplasia markers expression was assessed by RTqPCR, western blot and immunostaining. EMT functional properties were evaluated by invasion assays *in vitro*.

**Results**: *H. pylori* stimulated YAP1 and LATS2 in a coordinated biphasic pattern characterized by an early and transient YAP1 nuclear accumulation and activation. This activation was followed by LATS2 up-regulation leading to YAP1 phosphorylation and inactivation. Loss-of-function experiments showed that LATS2 restricts *H. pylori*-induced EMT markers expression, invasion, and expression of intestinal metaplasia markers. These results support a role for LATS2 in maintaining the epithelial phenotype of gastric epithelial cells by constraining *H. pylori*-induced preneoplastic changes.

**Conclusion**: *H. pylori* infection engages numbers of signaling cascades that alienate mucosa homeostasis, including the Hippo LATS2/YAP1 pathway. The Hippo signaling pathway appears as a protective pathway limiting the loss of gastric epithelial cell identity that precedes gastric carcinoma development.

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## P5.07 | Synchronous gastric neoplasm risk in early gastric cancer patients according to OLGA and OLGIM stages

**J. Lee**; Y. Kim; M. Kook; C. Kim; I. Choi

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**Objective**: We evaluated the proportion of synchronous gastric neoplasm in early gastric cancer (EGC) patients who underwent endoscopic submucosal dissection (ESD) according to the OLGA and OLGIM stages.

**Methods**: In this retrospective study, 495 patients who underwent ESD for EGC between July 2009 and December 2014 were included. OLGA and OLGIM stages were determined using scores of antrum and corpus lesser curvature biopsy samples assessed by the updated Sydney system. High-risk group included patients with OLGA or OLGIM stages III and IV.

**Results**: Of the 495 patients, 60 patients (12.1%; 35 cancer and 25 adenoma) had synchronous gastric neoplasm. OLGA stages were evaluated in 466 patients, and proportions of synchronous neoplasms were 5.3% (1/19) in stage 0, 9.1% (5/55) in stage I, 6.1% (5/82) in stage II, 12.7% (16/126) in stage III and 17.4% (32/184) in stage IV. The proportions of synchronous neoplasm were increased with higher OLGA stages ($P_{trend}$=0.009). The high-risk OLGA group had a higher proportion of synchronous neoplasm than low-risk group (15.5% vs 7.1%, respectively; $P$ = 0.012). Synchronous neoplasms were detected more frequently in patients with advanced OLGIM stages (2.9% [1/34] in stage 0, 8.2% [6/73] in stage I, 7.8% [7/90] in stage II, 11.5% [18/157] in stage III and 19.9% [28/141] in stage IV; $P_{trend}$ <0.001). The proportion of synchronous neoplasm was significantly higher in the high-risk OLGIM group than in the low-risk group (15.4% vs 7.1%, respectively; $P$ = 0.005).

**Conclusions**: Synchronous gastric neoplasms were more frequently detected in EGC patients with advanced OLGA and OLGIM stages.

J. Lee: None. Y. Kim: None. M. Kook: None. C. Kim: None. I. Choi: None.

## P5.08 | cfDNA mutation profile analysis for gastric cancer patients

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Cell-free DNA (cfDNA) is released into the bloodstream in various ways including the death of cells or by active secretion. New minimally invasive diagnostic procedures for circulating molecules are in demand because standard diagnostics are not able to analyze the cancer mutation profile changes over the course of treatment. However, there is a lack of comparative studies conducted in gastric cancer comparing tumor tissue DNA and cfDNA mutation profiles.

The aim of a study was to compare tumor tissue DNA and cfDNA mutation profiles. The study was approved by the Kaunas regional biomedical research ethics committee (No. Nr. BE-2-10). Gastric cancer tissue and blood were collected from 30 patients who were recruited at the Department of Gastroenterology, Lithuanian University of Health Sciences Hospital. Tumour tissue was obtained from the primary lesion of the resected specimen or biopsy and stored at −80°C. Peripheral blood was drawn using $K_2$EDTA tubes at admission (before surgery). Sequencing libraries were prepared using TruSeq Nano Libraries and samples of cfDNA pilot study were done in two replicates. Genomic DNA of tumor tissue and cfDNA were analyzed for mutations using xGen Pan-Cancer Panel (IDT). Libraries were pair-end sequenced on an Illumina NextSeq 500.

Overall, 16 patients had mutations detected in gastric cancer-related genes. Most frequently mutated genes in our study were TP53, BRCA2, NOTCH1, CHECK2, ERBB4, and KRAS.

Our results demonstrate that cfDNA reflects mutation profile in gastric cancer tissue DNA, therefore, may enable cfDNA analysis for monitoring disease stage of gastric cancer patients.

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## P5.09 | No progression of intestinal metaplasia following *H. pylori* eradication in an Irish cohort

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*Tallaght Hospital/Trinity College Dublin, Dublin, Ireland*

**Introduction**: Gastric cancer (GC) is the second leading cause of cancer-related death in the world. Most gastric adenocarcinomas are preceded by a cascade of well-defined precursor lesions, including intestinal metaplasia (GIM) and dysplasia. *H. pylori* is thought to be the instigating agent for this cascade. We aimed to investigate whether eradication of *H. pylori* could prevent progression from GIM to GC in an area of low incidence of GC.

**Methods**: All patients with GIM detected at gastroscopy in Tallaght University Hospital from 2008 to 2012 were identified in the hospital database. Follow-up data were evaluated until 31st December 2018.

**Results**: 58 patients who had *H. pylori* eradicated were followed up. Of those 54 had antral biopsies, 40 had corpus biopsies and 37 had biopsies of antrum and corpus. No progression to dysplasia or GC was noted, compared to 3% of the entire cohort. 28 patients were still noted to have GIM. Of 37 patients who had the recommended surveillance biopsies of antrum and corpus 23 still had GIM 14 and 14 had no evidence of GIM in any biopsies.

**Conclusion**: In this low GC incidence population eradicating *H. pylori* is a useful strategy to halt and possibly reverse progression of the cancer pathway.

A. O'Connor: None. E. Farrell: None. J. Weininger: None. A. Bowden: None. S. Crowther: None. D. McNamara: None. C. O'Morain: None.

## P5.10 | Comparison of treatment outcomes of endoscopic and surgical resections of gastrointestinal stromal tumors in the stomach: a propensity score-matched case-control study

**G. Kim**; K. Choi; H. Na; J. Ahn; J. Lee; K. Jung; D. Kim; H. Song; G. Lee; H. Jung; J. Kim

*Asan medical center, Seoul, Republic of Korea*

**Background/Aim**: We aimed to investigate the safety and efficacy of endoscopic resection compared to surgical resection of gastric gastrointestinal stromal tumors (GISTs).

**Methods**: Between June 2005 and August 2017, 55 patients underwent endoscopic resection and 403 patients underwent surgical resection for GISTs of 5 cm or less in the stomach at a tertiary care center. After a 1:1 propensity score matching using age, sex, tumor size, mitotic count, comorbidities, 48 patients were belonging to the endoscopic resection (ER) group and 48 patients were belonging to the surgical resection (SR) group. The clinical and oncological outcomes were compared between the two groups.

**Results**: The overall mean follow-up period was 46.4 ± 28.6 months in the ER group and 46.6 ± 37.1 months SR group. The R0 resection rate was 62.2% in the ER group where it was 100% in the SR group. The ER group had significantly shorter hospital stays (4.5 ± 2.9 vs 6.6 ± 3.6 days, $P = 0.004$) and procedure times (38.7 ± 24.7 vs 55.8 ± 23.2 minutes, $P < 0.001$). No recurrence or distant metastasis occurred in both groups during the follow-up period. Of all study patients (n = 458), 10 showed recurrence during a median follow-up time of 31.5 months. A high mitotic index (hazard ratio [HR] 20.21, $P < 0.001$) and tumor size (HR 2.57, $P = 0.014$) were predictors of recurrence but not the resection method or positive microscopic resection margin, tumor location.

**Conclusions**: ER is an effective and safe therapeutic method that might be comparable to SR for treating small sized (5 cm or less) gastric GISTs.

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## P5.11 | Role of *Helicobacter pylori* CagA in Casein kinase 2 mediated epithelial-mesenchymal transition in gastric cancer cells

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The pathogenic mechanism of gastric carcinogenesis by *H. pylori* remains unknown. Casein kinase 2 is a serine/threonine protein kinase. CK2 regulates many substrates and is involved in cell growth, proliferation, survival, angiogenesis, and invasion. Epithelial-to-mesenchymal transition (EMT) is involved in many signaling pathways, but the key regulatory kinases in this process have not been clearly identified. Although the role of CK2 catalytic subunits has remained largely uncharacterized, several studies have recently focused on regulator subunits in EMT. In this study, we analyzed the molecular mechanism related to gastric carcinogenesis by investigating the role of CK2 in EMT. Herein, the expression of CK2α was not altered, whereas CK2β decreased in CagA-dependent pathway. Moreover, expression of ectopic CK2β was downregulated by CagA. Also, the level of ubiquitinated CK2β were higher in HP60190 infected cells than in control cells. Thus, CK2β is degraded by the proteasomal pathway following CagA translocation of *H. pylori*. In addition, CagA binds both CK2α and CK2β, which resulted in the suppression of CK2β binding by infected HP60190, but does not suppress CK2α binding. Furthermore, downregulation of CK2β increased Snail as CK2 target genes, EMT-related marker in *H. pylori*-infected gastric cancer cells. Overall, CK2 tetramer subunits may control the function of CagA and EMT related genes, thereby regulating CagA-dependent gastric carcinogenesis. Taken together, the present study suggests that the CK2 regulatory subunit has diverse effect on CagA-dependent cellular processes. A pharmacological activator or activator of CK2β may have potential as a therapeutic agent for gastric cancer.

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## P5.12 | Association of long non-coding RNA polymorphisms with gastric cancer and atrophic gastritis

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**Introduction**: Many studies had proved that long non-coding RNA (lncRNA) single-nucleotide polymorphisms (SNPs) played an important role in the carcinogenesis.

**Aims & Methods**: The aim of this study was to examine associations of lncRNA rs217727, rs3200401, rs17840857, rs1054000, rs17694493, rs1333045, rs1011970 polymorphisms with gastric cancer (GC) and atrophic gastritis (AG) in European population. Gene polymorphisms were analyzed in 613 GC patients, 118 patients with AG and 476 controls from 3 tertiary centers in Germany, Lithuania and Latvia. Genomic DNA was extracted using salting out method from peripheral blood mononuclear cells. SNPs were genotyped by the real-time polymerase chain reaction. Associations between gene polymorphism and GC were evaluated using multiple logistic regression analysis with adjustment for sex, age and country.

**Results**: We observed a similar distribution of genotypes and allelic frequencies of all the polymorphisms between GC, AG patients and controls, except of rs17694493. The GG genotype of this polymorphism was more prevalent in AG patients compared to control group (3.4% and 0.6% respectively, $P = 0.033$). However, the frequency of the G allele in AG patients did not differ significantly from controls (11.9% and 14.0% respectively, $P > 0.05$). Logistic regression analysis revealed that only one polymorphism (rs17694493) was associated with increased risk of GC. Carriers of GG genotype had higher odds of GC when compared to CC genotype (OR – 4.93; PI 1.28 – 18.99, $P = 0.02$).

**Conclusion**: rs17694493 SNP is associated with increased risk of GC, while polymorphisms of other analyzed SNPs are not linked with the presence of GC.

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## P5.13 | Pan-genomic approach to identify new serological biomarkers for *Helicobacter pylori* related outcomes

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*H. pylori* is a widespread human pathogen and the leading risk factor for gastric cancer. Yet, most infections remain asymptomatic. To stratify the individual risk potential, serological biomarkers would be of great advantage. So far, antibodies to CagA seem to be most promising, since several studies demonstrated associations with increased gastric cancer incidences. In some countries however, seropositivity to CagA is high overall and therefore not suitable to identify high-risk groups. To efficiently target patients at risk, new biomarkers are required.

We generate high-density antigen microarrays, combining multiple spotting technique with cell-free, on-chip protein expression. Considering high strain-specific genetic diversity, we represent the entire pan-genome of *H. pylori* by systematically aligning sequenced strains, clustering possible antigens and minimizing redundancy. Biomarkers associated with gastric cancer are identified by immunoassays with sera derived from case-control studies. Protein alignments of 120 strains were processed by Markov Clustering Algorithms. Strain 26695 was used as a scaffold for most expression constructs. By adding accessory genes from locally diverse isolates, the microarray was complemented to express approximately 75% of the known *H. pylori* pan-genome. Initial testing of a case-control study on a 26695 microarray led to the confirmation of established, and the identification of new biomarkers. Screening of prediagnostic samples from case-control studies nested in prospective cohorts on the pan-genomic microarray is ongoing.

Our *H. pylori* microarray offers a platform for unbiased identification of new serological biomarkers. Given the easily adaptable workflow, antibody responses linked to diverse *H. pylori*-related outcomes can be systematically identified.

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## P5.14 | The molecular signatures of pre-cancerous metaplasia in the stomach

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The gastric epithelium is geographically heterogeneous, containing functionally distinct pyloric and corpus mucosal lineages. Active chronic gastritis, most often caused by *Helicobacter pylori* infection, progresses to multifocal atrophic gastritis with loss of parietal cells and chief cells and the appearance of metaplastic lineages that are predisposed to neoplastic transformation. Thus, oxyntic atrophy, the loss of parietal cells, represents the critical alteration of the gastric mucosal most associated with gastric pre-neoplasia. The loss of parietal cells leads to the development of two identifiable metaplasia is associated with gastric cancer: intestinal metaplasia (IM) and spasmolytic polypeptide-expressing metaplasia (SPEM). Recently, our studies showed that SPEM is an early metaplastic change in the corpus of the stomach in the setting of amphiregulin deficiency. IM evolved in the setting of precedent SPEM, suggesting that IM arises from SPEM. IM is not neoplasm itself but recognized as precancerous lesion of gastric cancer. Investigators reported IM is clonal and share founder mutation with gastric dysplasia. IM and gastric dysplasia could be genetically related, featuring the clonal origin of dysplasia from IM. We also identified the markers for gastric metaplastic lineages expressed in different locations and distributions in IM, including ACE2, MUC13, CDH17, OLFM4, MUC5AC, REG4, KRT20, LGALS4, AKR1B10, and Paneth cell expression at the bases of glands (LYZ, DEFA5, DEFA 6). Pathologic characteristics, molecular features and clinical implications of IM will be addressed and provide our future perspectives in this research field.

K. Nam: None.

## P5.15 | Predictive model for endoscopic ultrasonography accuracy of invasion depth in early gastric cancer

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**Background/Aims**: Endoscopic ultrasonography(EUS) have been used to predict invasion depth of early gastric cancer(EGCs). However, role of EUS is still controversial. This study is to analyze clinicopathologic factors which affect EUS accuracy and to develop predictive model for EUS accuracy.

**Methods**: 1,058 lesions were analyzed. We evaluated accuracy of EUS by comparing EUS T staging and final histopathologic staging. We created a model for prediction accuracy and validated by the area under the curve(AUC) and using split-sample method. We assigned the score and created a nomogram which can calculate the prediction value with total score.

**Results**: Overall accuracy of EUS for T staging was 69.1%(731/1058) when divided into T1a, T1b, and over T2. Multivariable model for prediction accuracy was made using 80% splitting method. A 20% test set showed AUC of 0.7066 (95%CI, 0.6294-0.7839). We assigned risk score for discordance and made nomogram to make a system that can calculate prediction value with total score. Risk scores assigned for variables are as follows: undifferentiated histology, tumor size(>10 mm), ulcer, lower body, gross morphology. The expected prediction value through nomogram is listed in table 1.

**Conclusion**: We developed a validated model predicting lesions with low EUS accuracy in T staging of EGC. We could reflect this model to decide ESD candidates by selecting patient group who needs to be careful in interpreting EUS result.

**TABLE 1.** Risk for discordance of EUS by assigned score

| Nomogram total points | Predicted value |
|---|---|
| 26 | 0.10 |
| 66 | 0.20 |
| 93 | 0.30 |
| 116 | 0.40 |
| 136 | 0.50 |
| 156 | 0.60 |
| 178 | 0.70 |
| 205 | 0.80 |
| 246 | 0.90 |
| 283 | 0.95 |

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## P5.16 | Efficacy of radiotherapy for localized gastric mucosa-associated lymphoid tissue lymphoma

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**Background and aims**: The treatment strategy in patients with gastric mucosa-associated lymphoid tissue (MALT) lymphoma who are *Helicobacter pylori*-negative or unresponsive to *H. pylori* eradication therapy remains still controversial. Therefore, we aimed to investigate the clinical efficacy of radiotherapy for localized gastric MALT lymphoma.

**Methods**: This was a retrospective single-center study based on the medical records of 26 patients who underwent radiotherapy for gastric MALT lymphoma at Pusan National University Hospital between April 2009 and August 2018. Radiotherapy was administered 17 times, with a total dose of 30.6 Gy and fraction size of 1.8 Gy. All the patients were treated with opposed anterior and posterior fields to the stomach and perigastric lymph nodes.

**Results**: Among 26 patients, 25 were in Ann Arbor staging IE1 and one was in IE2. Twenty-three patients without a complete remission (CR) after *H. pylori* eradication therapy or chemotherapy received radiotherapy as the secondary treatment, and one patients with *H. pylori*-positive gastric MALT lymphoma and two with *H. pylori*-negative gastric MALT lymphoma received radiotherapy as the primary treatment. CR of MALT lymphoma was achieved in all 26 patients (100%). Only mild adverse events such as nausea and dyspepsia were noted during radiotherapy. During the median follow-up period of 37.6 months (range, 8-127 months), there was no recurrence in any patients.

**Conclusions**: Radiotherapy may be an effective treatment option in patients with *H. pylori*-negative MALT lymphoma or *H. pylori*-positive MALT lymphoma that is not responsive to *H. pylori* eradication therapy.

G. Kim: None. M. Lee: None. B. Lee: None. G. Song: None.

## P5.17 | Efficacy of the Kyoto classification of gastritis to identify the risk of dysplasia and early gastric cancer in *Helicobacter pylori* patients

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**Background**: Infection with *Helicobacter pylori*(*H. pylori*) is an important factor in the development of gastric cancer. The gastric cancer reported to develop in 0.1 to 3% of *H. pylori* infected patients. The Kyoto classification of gastritis developed to categorize the endoscopic characteristics of *H. pylori* infection-associated gastritis and

identify patterns associated with a risk of gastric cancer. We investigated whether the Kyoto classification of gastritis can effectively identify the risk of dysplasia and early gastric cancer(EGC) in *H. pylori* patients.

**Methods**: A total 146 patients with *H. pylori*-positive gastritis alone(Group A, n = 86) and *H. pylori* patients with dysplasia or EGC(Group B, n = 60) were endoscopically graded according to Kyoto gastritis classification for atrophy, intestinal metaplasia(IM), fold hypertrophy, nodularity, and diffuse redness.

**Results**: No significant differences were noted in age and sex. The Kyoto gastritis scores of atrophy and intestinal metaplasia in Group B were significantly higher than in Group A (1.8 ± 0.5 VS 1.3 ± 0.5 in atrophy, $P < 0.001$; 1.55 ± 0.7 VS 0.7 ± 0.8 in IM, $P < 0.001$). No significant differences were noted in the rates of fold hypertrophy, nodularity, and diffuse redness. In a multivariate analysis, the risks for dysplasia or EGC increased with IM (30.125, 6.688-135.698, $P < 0.001$) and over 65 years old (4.440, 1.778-11.089, $P = 0.001$).

**Conclusions**: The scores of atrophy and intestinal metaplasia in the Kyoto gastritis classification may be useful for endoscopic detection of patients at high risk of developing dysplasia or EGC. *H. pylori*-positive patients with IM or over 65 years old should be observed carefully during endoscopy.

Y. Myung: None.

## P5.18 | The association between polymorphism in HLA-A, HLA-B, HLA-DR and DQ genes of gastric cancer and duodenal ulcer patients with CagL positivity among CagA-positive *Helicobacter pylori* strains

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**Background**: Cytotoxin-associated gene L (CagL) has been shown to play a role for the injection of CagA into gastric epithelial cells. Polymorphisms in HLA genes are associated with the development or prevention of gastric cancer in *H. pylori*-infected individuals. We aimed to evaluate the association between polymorphism in HLA-A, HLA-B, HLA-DR and DQ genes of gastric cancer and duodenal ulcer patients and cagL positivity among cagA-positive *H. pylori* strains.

**Methods**: The study and control groups were formed from 94 *H. pylori* strains (44, gastric cancer, 50 duodenal ulcer patients) and 86 *H. pylori* strains (50, non-ulcer dyspepsia patients, 36 individuals with normal gastrointestinal system), respectively. cagA and cagL were determined by PCR method. DNA from peripheral blood samples was obtained by EZ-DNA extraction kit. HLA-A, -B, -C, -DRA1, DRB1, DRQA1 and DRQB1 loci genotyping were performed by eRES SSO HLA Typing Kits.

**Results**: HLA-A*01, HLA-A*02, HLA-A*03, HLA-B*35, HLA-DQA1*01, HLA-DQA1*02, HLA-DQA1*06 and HLA-DQBA1*05 alleles were detected significantly higher in study group due to the cagA+cagL. HLA-DQA1 01 [$P = 0.001$, OR:2.415 95% CI (1.439-4.055)] and HLA-A 02 ($P = 0.017$, OR:1.979, 95% CI (1.128-3.473)] were detected as independent risk factors for gastric cancer and duodenal ulcer.

**Conclusions**: HLA-A*02 and HLA-DQA1*01 alleles exhibited similar ORs. We may suggest that individuals with HLA-A*02 and HLA-DQA1*01 alleles may have 1.97 and 2.4 folds higher gastric cancer or duodenal ulcer risk than individuals with other HLA alleles when infected with *H. pylori* strains with cagA+cagL.

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## P5.19 | The relationship between polymorphism in HLA-A, HLA-B, HLA-DR and DQ genes of gastric cancer and duodenal ulcer patients with *Helicobacter pylori* cagA/vacA s1m1 genotype

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**Background**: *Helicobacter pylori* strains with cagA/vacAs1m1 genotype are significantly associated with gastric cancer. Polymorphisms in HLA genes are also associated with the development or prevention of gastric cancer in *H. pylori*-infected individuals. We aimed to evaluate the association between polymorphism in HLA-A, HLA-B, HLA-DR and DQ genes of gastric cancer and duodenal ulcer patients and *H. pylori* cagA/vacAs1m1 genotype.

**Methods**: The study and control groups were formed from 94 *H. pylori* strains (44, gastric cancer, 50 duodenal ulcer patients) and 86 *H. pylori* strains (50, non-ulcer dyspepsia patients, 36 individuals with normal gastrointestinal system), respectively. cagA/vacAs1m1 genotype was determined by PCR method. DNA from peripheral blood samples was obtained by EZ-DNA extraction kit. HLA-A, -B, -C, -DRA1, DRB1, DRQA1 and DRQB1 loci genotyping were performed by eRES SSO HLA Typing Kits.

**Results**: vacAs1m1 genotype were detected in 34 (36.1%), and 12 (13.9%) of the study group and control group strains, respectively. HLA-DQA1*01, HLA-DQA1*03, HLA-DQB1*05 and HLA-A1*02 alleles were detected significantly higher in study group due to the cagA/vacAs1m1 genotype. Only HLA-DQA1 01 [$P = 0.002$, OR: 2.071, 95% CI (1.311-3.271] and HLA-A 02 [$P = 0.039$, OR:1.672,

95% CI (1.027-2.721] alleles with cagA/vacAs1m1 genotype were detected as the risk factors for gastric cancer or duodenal ulcer due to caga/vacAs1m1 genotype

**Conclusions**: HLA-DQA1*01 and HLA-A*02 alleles indicated similar ORs (2.071 and 1.672). We may suggest that individuals carrying cagA/vacAs1m1 genotype *H. pylori* with these alleles may have 2 and 1.67 folds higher gastric cancer or duodenal ulcer.

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## P5.20 | Translational relevance of ITGA5 expression in *H. pylori* infection, preneoplastic conditions and gastric cancer

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**Introduction**: Integrin alpha5beta1 (ITGA5) expression has been linked to gastric cancer (GC) and the translocation of cytotoxin-associated gene A (CagA). However, little knowledge on ITGA5 expression in various stages of gastric carcinogenesis is available. Aim of the study was to examine ITGA5 expression based on preneoplastic gastric pathologies and *H. pylori* infection.

**Methods**: Gastric antrum biopsies were obtained from 146 patients with normal mucosa (N), chronic non-atrophic gastritis (CNAG), atrophic gastritis (AG) and gastric carcinoma (GC). Additional tumor biopsies were obtained from the GC-patients. The *H. pylori* status was determined based on serology, histopathology and microbiological cultivation, as well as the CagA and VacA genotype. Ex vivo CD4+ T cells and in vitro AGS cell line models were used to estimate the impact of *H. pylori* on ITGA5 expression.

**Result**: Paired comparison of non-tumorous antrum and tumor biopsies of the GC patients revealed no significant difference in ITGA5 expression. Similar results were obtained in antrum biopsies between N- and GC-groups. In general, there was no clear correlation between *H. pylori* status and ITGA5 expression. The subgroup analysis revealed that the CNAG/Hp- patients expressed significantly more ITGA5 than N, AG/Hp- or GC/Hp+ patients ($P = 0.0314$). Mucosal CD4+ T-cells and AGS cells showed no increased ITGA5 expression based on *H. pylori* status.

**Conclusion**: In this work we did not observe any potential expression pattern of ITGA5 in preneoplastic conditions or gastric cancer. Neither mucosal CD4+ ex vivo nor in vitro co-cultivation experiments supported the translational role of ITGA5 in gastric carcinogenesis.

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## P5.21 | Risk factors of early and advanced gastric cancer: a 8 years population study in northern Italy

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**Introduction and aim**: Gastric cancer (GC) in Italy is the fifth cause of death for neoplasia. Aim was to extrapolate epidemiological, pathological and clinical data, to clarify risk factors and the proportion of early diagnosis.

**Material and Methods**: The study was based on data analysis on GC in two areas: Parma and Ulss7 Altovicentino, during 2011-2017. A database was created where clinical features and the association with some risk factors were investigated.

**Results**: We found few early diagnoses (10.5% Parma vs 6% Ulss7) on 421 pts in Parma and 165 in Ulss7.

About 90 cases/year were found in Parma and 30 in Ulss7. Mean age was of 82.2 yrs in Parma, compared to 72 years.

Chronic atrophic gastritis was found in 95% of cases in Parma and in 81% in Ulss7. Data shown more cardia localizations (20%) in Ulss7 compared to Parma (8.3%). An increase in "signet ring" histotype was found in Ulss7 compared to Parma (27.8% vs 13.3%). Concerning risk factors in Ulss7 area, smoking, alcohol, drugs (PPI and statins), familiarity and co-morbidities, only continuous PPI therapy demonstrated a relevant association, with no causal link.

**Conclusions**: GC frequency was higher in Parma (387 vs 175: 100,000), as mean age (82.2 yrs vs 72 yrs). There were different percentages of cardia cancers and "signet ring" histotype. The most alarming data was the low percentage of early diagnosis. Thus, early diagnosis of precancerous lesions to avoid the future onset of GC is crucial.

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## P5.23 | Discrepancy of endoscopic atrophic gastritis between linked color imaging and white light imaging

**T. KaWai**; K. Takahashi; Y. Kawai; H. Yamaguchi; N. Nagata; K. Yanagisawa; N. Uemura

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Recently image enhanced imaging (IEE) is conducted in endoscopic diagnosis. Endoscopic gastric atrophy is a risk factor of gastric

cancer. Linked color imaging (LCI) is one of IEE which processes images to improve color separation in red regions of image of mucosal blood vessels. We compared endoscopic gastric atrophy between LCI and white light imaging (WLI).

**Subjects and Methods**: Subjects were 53 patients who were conducted transnasal endoscopy equipped LCI system for upper GI screening. Mean age was 64.7 ± 13.7, male/female ratio was 27/26. We diagnosed endoscopic gastric atrophy using WLI and LCI observation in accordance with kimura & Takemoto classification (C-0, C-1, C-2, C-3, O-1, O-2, O-3). We also evaluated endoscopic atrophic image based on L*a*b* color value.

**Result**: Number of grade of endoscopic gastric atrophy were C-0:27, C-1:4, C-2:6, C-3:5, O-1:6, O-2:5, O-3:0 in WLI observation respectively, on the other hand C-0:5, C-1:21, C-2:5, C-3,:5, O-1:3, O-2:13, O-3:1 in LCI observation. With reference with score of L*a*b* color value in atrophic lesion, L*:50.7 ± 15.6, a*:27.3 ± 5.7, b*:34.9 ± 0.7 using WLI, L*:60.3 ± 1.4, a*:11.7 ± 6.4, b*:28.8 ± 4.9 using LCI respectively.

**Conclusion**: Endoscopic gastric atrophy was observed more severe using LCI than WLI. This reason is related that LCI system makes it easier to identify red and discolored lesion.

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## P5.24 | Optimal initial work-up in patients with superficial primary gastric MALT lymphoma

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**Background**: Prognosis of gastric MALT lymphoma is favorable, especially when there is no lymph node (LN) metastasis. We investigated the incidence and occurrence site of LN metastasis in superficial gastric MALT lymphoma.

**Methods**: Retrospective analysis of gastric MALT lymphoma from 1995 to 2016 was performed. A total of 452 patients with gastric MALT lymphoma confined to mucosa or submucosa on EUS was enrolled. The incidence and occurrence site of LN metastasis was evaluated.

**Results**: Out of 452 patients, the majority of patient (n = 436, 96.5%) were LN negative in initial staging work-up using CT scanning. Sixteen patients (3.5%) were LN positive and there was no difference in clinical characteristics between two groups except for extent of lymphoma involvement. Among 41 patients who underwent only abdominal/pelvic CT (APCT), LN metastasis was detected in one patient (2.4%). There were eight LN metastases in patients who underwent both APCT and chest CT (n = 238, 3.4%). Among 171 patients who underwent APCT, chest CT and neck CT all, seven LN metastasis was detected (4.1%). The detection rates for each CT were as follows: 13 out of 450 patients in Abdominal CT (2.9%), 6 out of 408 patients in chest CT (1.5%), one out of 171 patients in neck CT (0.6%).

**Conclusion**: The incidence of LN metastasis was low in gastric MALT lymphoma patients confined to mucosa or submucosa on EUS. It might be necessary to develop optimal strategy of initial work-up in patients with primary gastric MALT lymphoma, who are considered to have superficial infiltration on EUS.

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## P5.25 | Digital endosonographic image analysis-based scoring system for gastric mesenchymal tumors

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**Background**: When gastric mesenchymal tumors (GMTs) measuring 2-5 cm in size are found, whether to undergo further treatment or not is controversial. Endoscopic ultrasonography (EUS) is useful for the evaluation of malignant potential of GMTs, but has limitations, such as subjective interpretation of EUS images. Therefore, we aimed to develop a scoring system based on the digital image analysis of EUS images to predict gastrointestinal stromal tumors (GISTs).

**Methods**: We included 103 patients with histopathologically proven GIST, leiomyoma or schwannoma on surgically resected specimen who underwent EUS examination between January 2007 and June 2018. After standardization of the EUS images, brightness values, including the mean ($T_{mean}$), indicative of echogenicity, and the standard deviation ($T_{SD}$), indicative of heterogeneity, in the tumors were analyzed.

**Results**: Age, $T_{mean}$, and $T_{SD}$ were significantly higher in GISTs than in non-GISTs. The sensitivity and specificity were almost optimized for differentiating GISTs from non-GISTs when the critical values of age, $T_{mean}$, and $T_{SD}$ were 57.5 years, 67.0, and 25.6, respectively. A GIST predicting scoring system was created by assigning 3 points for $T_{mean}$ ≥67, 2 points for age ≥ 58 years, and 1 point for $T_{SD}$ ≥26. When GMTs with 3 points or more were diagnosed as GISTs, the sensitivity, specificity, and accuracy of the scoring system were 86.5%, 75.9%, and 83.5%, respectively.

**Conclusions**: The scoring system based on the information of digital image analysis is useful in predicting GISTs in case of GMTs that are 2-5 cm in size.

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## P5.26 | Comparison between redo endoscopic treatment and surgery in patients with locally recurrent gastric neoplasms

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**Background**: Treatment of locally recurrent gastric neoplasms after endoscopic resection remains challenging. We investigated the efficacy and safety of treatment options for recurrent gastric neoplasms localized to the scar of previous endoscopic submucosal dissection (ESD).

**Methods**: The clinicopathological characteristics and treatment outcomes of patients who underwent endoscopic treatment or surgery for recurrent gastric neoplasms between June 2010 and May 2017 were retrospectively reviewed.

**Results**: Of the 92 patients included, 74 underwent endoscopic treatment (51 redo ESD, 23 argon plasma coagulation [APC] ablation) and 18 underwent surgery. The redo ESD procedure time was significantly longer than that of the primary ESD (31.0 vs 22.0 minutes, $P$ = 0.018). Overall, adverse events occurred in 11 patients (12.0%), with the incidence being significantly higher in the surgery group (27.8% vs 8.1% in the endoscopic treatment group, $P$ = 0.036). Local recurrence-free survival rates were 81.1% for the endoscopic treatment group (86.3% and 69.6% for redo ESD and APC groups, respectively) and 100% for the surgery group (log rank $P$ = 0.033). Logistic regression analysis showed that tumor size >12.5 mm and tumors located in the upper two thirds of the stomach were associated with non-curative resection after redo ESD.

**Conclusions**: Endoscopic treatment could be an effective and safe alternative to surgery for selected patients with gastric neoplasms recurring at the scar of previous ESD. Especially, patients having small lesion located in distal part of stomach could be a good candidate for redo ESD.

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## P5.27 | Endoscopic submucosal dissection versus surgery for undifferentiated-type early gastric cancer: A systematic review and meta-analysis

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**Background**: Endoscopic submucosal dissection (ESD) for treating undifferentiated-type early gastric cancer (UD-EGC) is controversial. The objective of this study was to perform a meta-analysis to compare long-term outcomes of ESD and surgery for UD-EGC.

**Methods**: PubMed, Cochran Library, and EMBASE were used to search for relevant researches comparing ESD and surgery for UD-EGC. Methodological quality of included publications was evaluated using the Risk of Bias Assessment tool for Non-randomized Studies. Overall survival rate, recurrence rate, adverse event rate, and complete resection rate were determined. Odds ratio (OR) and 95% confidence interval (CI) were also evaluated.

**Results**: This meta-analysis enrolled five studies with 376 and 1148 participants undergoing ESD and surgery, respectively. There was no significant difference in overall survival rate between ESD and surgery groups (OR: 1.76, 95% CI: 0.55-5.66, $P$ = 0.34). However, ESD was associated with higher recurrence rate (OR: 11.57, 95% CI: 5.07-26.39, $P$ < 0.001) and lower complete resection rate (OR: 35.08, 95% CI: 9.39-131.11, $P$ < 0.001). Adverse event rate was similar between the two groups (OR: 0.95, 95% CI: 0.46-1.96, $P$ = 0.88).

**Conclusion**: ESD with meticulous surveillance esophagogasroduodenoscopy in patient with UD-EGC might be as effective and safe as surgery. Further randomized, controlled studies in large scale from additional legions are required to confirm these findings.

B. Kim: None. D. Ma: None. J. Kim: None.

## P5.28 | Usefullness of L-Cysteine for the recovery of gastric function in CAG patients: A 5-years follow-up study

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**Background and aim**: Acetaldehyde is a class one chemical carcinogen. L-Cysteine inactivates Acetaldehyde by covalent binding. Aim was to verify modifications of functionality and symptoms in CAG patients, treated with L-Cysteine in a long-term follow-up.

**Materials and Methods**: Overall, 326 consecutive patients (205 F; mean age: 47; range: 26-77) were enrolled and all followed-up for at least 3 years (215 pts for 4 and 102 pts for 5). Everyone took L-Cysteine 100 mg, 3 pills/day. CAG was diagnosed at baseline through EGD with biopsies, classified with O.L.G.A. staging and serology, assessing PG1 levels less than 25 mcg/L and G-17 levels more than 12 pg/L. Everyone underwent yearly serology, Global Symptomatic Score (GSS) based on 4 symptoms (epigastric fullness, nausea, bloating, post-prandial discomfort), 3 levels of severity per each (mild, moderate, severe) and Visual Analogue Scale (VAS), ranging from 1

to 10 (10: absence of pain and 1: unbearable pain). A control group of 128 CAG patients (F: 68; mean age: 56; range: 31-69), was off-therapy (only symptomatic drugs) and underwent serology, GSS and VAS for 3 years.

**Results**: Results are shown in Table 1 and Table 2.

**Conclusions**: L-Cysteine seems to improve functionality and symptoms of CAG during a 5-years follow-up.

| | Baseline | T1 | T2 | T3 | T4 | T5 |
|---|---|---|---|---|---|---|
| l-Cysteine group | | | | | | |
| PG1 (mcg/dL) | 14 | 21 | 23 | 22 | 24 | 23 |
| G-17 (pg/L) | 38 | 27 | 24 | 21 | 19 | 17 |
| VAS | 5 | 8 | 7 | 8 | 9 | 8 |
| GSS | 8 | 4 | 3 | 5 | 4 | 3 |
| Control group | | | | | | |
| PG1 (mcg/dL) | 12 | 11 | 13 | 12 | | |
| G-17 (pg/L) | 44 | 39 | 45 | 47 | | |
| VAS | 9 | 10 | 8 | 9 | | |
| GSS | 4 | 5 | 3 | 4 | | |

F. Di Mario: None. A. Barchi: None. M. Russo: None. M. Franceschi: None. N. Dal Bò: None. R. Cannizzaro: None. C. Miraglia: None. A. Tursi: None. G. Brandimarte: None. P. Crafa: None. L. Franzoni: None. M. Rugge: None.

## P5.29 | *H. pylori*-miRNA interaction in gastric cancer tissues: First prospective study from Turkey

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*Helicobacter pylori* (*H. pylori*) is involved in the etiology of gastric cancer (GC). miRNAs are short RNAs that regulate gene expression by marking mRNAs for degradation. miRNAs are involved in tumorigenesis, metastasis, and cell proliferation. We aimed to investigate the miRNA expression profiles of tissues from *H. pylori* (+) and (-) GC patients. Forty GC patients, 20 *H. pylori* (+) and 20 *H. pylori* (-), and a healthy control group were included. The miRNA expression levels were investigated by microarrays and quantitative RT-PCR. We detected 9 upregulated and 4 downregulated miRNAs by microarray. We selected 5 upregulated and 5 downregulated miRNAs for the quantitative RT-PCR assay. The relative fold changes of miRNAs in the cancerous tissue and non-tumor mucosa specimens of *H. pylori* (+) GC patients for hsa-miR-194 were 4.24- and 3.83-fold higher, respectively, whereas the hsa-miR-145 expression levels were downregulated 0.33-fold and 0.43-fold, respectively, in the same group. The presence of *H. pylori* significantly upregulated hsa-miR-194 and downregulated hsa-miR-145 expression levels in *H. pylori* (+) GC cases, compared to *H. pylori* (-) GC cases. Regional differences in the virulence of *H. pylori* strains may also be involved in the up- or down-regulation of miRNA expression levels.

B. Kocazeybek: None. S. Demiryas: None. O. Uysal: None. D. Ozbey: None.

## P5.30 | The expression of paraoxonase 1 in the *Helicobacter pylori* infection and gastric carcinoma

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**Background**: High doses and/or inadequate removal of reactive oxygen species result in oxidative stress, which may cause severe metabolic malfunctions and damage to biological molecules including tissue DNA. Paraoxonase 1 (PON1) is one of the endogenous free radical scavenging systems in the human and believed to be involved in the protection against oxidative stress. But there was no study about differential PON1 expression in *H. pylori* infection. In this study, we investigated the changes of PON1 expression in the *H. pylori* infection and in the gastric carcinoma.

**Methods**: To investigate the effect of *H. pylori* infection on the expression of PON1, the gastric tissues from eighteen patients with *H. pylori* infection were used before and after eradication. The expression of PON1 was also investigated in 109 cases of the gastric carcinoma and adjacent non-tumor area. The degree of oxidative stress in the tissues was evaluated by malondialdehyde (MDA).

**Results**: The intensity of immunohistochemical stain on PON1 and MDA was significantly higher in pre-eradication state compared to post-eradication of *H. pylori* (1.83 vs 1.11 and 1.77 vs 1.05, $P < 0.05$, respectively). The expression of PON1 and MDA in *H. pylori* infection correlated significantly ($r = 0.586$, $P = 0.001$). The intensity of MDA was significantly higher in tumor than adjacent non-tumor area (1.22 vs 0.39, $P < 0.05$). However, intensity of PON1 showed no significant difference.

**Conclusion**: Paraoxonase 1 may be one of antioxidant enzyme in *H. pylori* induced gastritis. The role of paraoxonase 1 may need further study to conclude in the gastric carcinoma.

S. Kim: None. J. Kim: None.

## P5.31 | Prediction of chronic atrophic gastritis and gastric neoplasms by serum pepsinogen assay; systematic review and meta-analysis of diagnostic test accuracy

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Serum pepsinogen assay (sPGA), which reveals serum pepsinogen I (PG I) concentration and ratio of PG I/PG II, is a non-invasive test for predicting chronic atrophic gastritis (CAG) and gastric neoplasms. Although various cut-off values have been suggested, PG I ≤ 70 ng/mL and PG I/PG II ≤ 3 have been proposed. However, previous meta-analyses reported insufficient systematic reviews and only pooled outcomes, which cannot determine the diagnostic validity of sPGA with a cut-off value of PG I ≤ 70 ng/mL and/or PG I/PG II ≤ 3. We searched the core databases (MEDLINE, Cochrane Library, and Embase) from their inception to April 2018. Fourteen and 43 studies were identified and analyzed for the diagnostic performance in CAG and gastric neoplasms, respectively. Sensitivity, specificity, diagnostic odds ratio, and area under the curve with a cut-off value of PG I ≤ 70 ng/mL and PG I/PG II ≤ 3 to diagnose CAG were 0.59, 0.89, 12, and 0.81, respectively and to diagnose gastric cancer (GC) were 0.59, 0.73, 4, and 0.7, respectively. Methodological quality and ethnicity of enrolled studies were found to be the reason for the heterogeneity in CAG diagnosis. Considering the high specificity, non-invasiveness, and easily interpretable characteristics, sPGA has potential for screening CAG or GC.

G.H. Baik: None. C.S. Bang: None.

## P5.32 | Paraneoplastic manifestations could be predictors to determine prognosis of gastric adenocarcinoma

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**Background**: Gastric adenocarcinoma is an important cancer and lead to significant number of deaths worldwide. The purpose of this study was to evaluate prevalence and clinical manifestations of paraneoplastic syndromes related to gastric cancer in large retrospective cohort study in Thailand.

**Methods**: This retrospective cohort study was conducted in Thammasat University Hospital, Thailand between January 2010-July 2018. Clinical information, laboratory findings, endoscopic features, histological examinations, complications and treatment outcomes were extensively reviewed and all patients were monitored for at least 5 years after diagnosis of gastric cancer.

**Results**: Total of 210 gastric tumor patients were enrolled, of which gastric adenocarcinoma was diagnosed in 100 patients (57 males, 43 females, mean age = 61 years). The common presenting symptoms were dyspepsia(53%), weight loss(57%), and loss of appetite(38%). Male patients had significant higher history of smoking (93.3% vs 6.7%, *P* = 0.03, OR = 3.94, 95%CI 1.04-14.84) and more commonly presented with upper gastrointestinal bleeding (83.3% vs 18.8%, *P* = 0.001, OR = 16.41, 95%CI = 2.03-132.49) than female. Common paraneoplastic manifestations were hyponatremia (63%), thrombocytosis (33%) and eosinophilia (7%). Interestingly, eosinophilia was significantly more common in early stage, while hyponatremia and thrombocytosis were more prevalence in advanced stage (25% vs 6%, 68.5% vs 0%, and 35.9% vs 0%, all *P*-value < 0.05, respectively). 5-year survival was poorer in patients with hyponatremia, but was better in patients with eosinophilia compared to patients without these conditions(6.4%vs.13.0%, and 9.1%vs.0%, respectively).

**Conclusion**: Paraneoplastic syndromes related to gastric adenocarcinoma were not uncommon especially hyponatremia, eosinophilia and thrombocytosis. These paraneoplastic manifestations might be predictors to determine prognosis of gastric cancer patients.

R. Vilaichone: None. P. Poonyam: None. V. Mahachai: None. P. Chotivitayatarakorn: None.

## P5.33 | Gastric MALToma studied with FDG-PET: A comparison with endoscopic findings

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This study evaluated the diagnostic efficacy of fluorine-18 fluorodeoxyglucose PET/CT (F-18 FDG PET/CT) for patients with gastric mucosa-associated lymphoid tissue (MALT) lymphoma and examined the association between FDG avidity and the endoscopic lesions.

From January 2000 to December 2018, consecutive patients with stage-I gastric MALT lymphoma were enrolled in single centre retrospectively. A total of 131 patients were diagnosed with gastric MALT lymphoma. The median age of the patients was 58 years (20-81 years). There were fewer male than female (M:F, 48:83) and male to female ratio was 1:1.7.

Among the patients diagnosed with gastric MALT lymphoma, 19 who underwent a PET/CT for gastric MALT lymphoma were semi-quantitatively and qualitatively tested for FDG avidity of lesions in the stomach. Retrospectively collected data was analyzed to investigate the endoscopic findings between the patients with positive F-18 FDG PET/CT scans and those with negative scans.

11 of the 19 patients showed FDG avidity. When comparing the size of lesions in the stomach, the patients with FDG avidity had significantly larger lesions than those without (30.1 mm vs 15.0 mm, *P* = 0.03). According to the endoscopic finding of the lesions, FDG avidity was pronounced with 83% of the protruding tumors, and

100% of the erosive-ulcerative types, which are a type of depressed tumors.

When gastric MALT lymphoma is large and the macroscopic appearance of a lesion is that of a protruding tumor or erosive-ulcerative type of depressed tumor, there is a high probability that such patients may have a positive F-18 FDG PET/CT scan.

S.R. Jee: None. S.Y. Seol: None. S.H. Lee: None. H.S. Lee: None.

## P5.34 | Clinical predictors and survival rates of diffuse and intestinal type of gastric cancer patients: A*5-year longitudinal study*

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**Aim**: The objective of this study was to compare clinical characteristic, endoscopic findings, and survival rate between diffuse and intestinal type gastric cancer in Thailand.

**Method**: From September2011-October2018, this *retrospective longitudinal study* was performed in Thammasat University Hospital, Thailand. Baseline characteristic, the clinical manifestations, endoscopic findings, histology, and survival rate of gastric cancer were extensively reviewed and all patients were receiving robust observed for >5 years.

**Results**: 220 gastric tumor patients were enrolled, there were 100 patients with gastric adenocarcinoma(45.5%) included in this study(57 men, 43 women, mean age = 62 years). There were 38% diffuse type and 61% intestinal type gastric adenocarcinoma. Common presenting symptom was weight loss(57%), dyspepsia(53%) and loss appetite(33%) in both group. Patients with diffuse type was significantly younger than intestinal type(mean age 52vs66, *P*-value < 0.01, 95%CI7.6-19.1). Intestinal type gastric cancer presented with anemia significantly more frequently than diffuse type (66.7%vs.33.3%, *P*-value = 0.03, OR3.1, 95%CI 1.09-9.01; mean hematocrit 28.3 ± 6.2vs 31.2 ± 6.9, *P*-value = 0.03, respectively). Interestingly, fundus and gastric body were more commonly infiltrated by diffuse type than intestinal type gastric cancer(26.9%vs.4.8%, *P*-value = 0.04, and 71.4%vs.17.4%, *P*-value < 0.01, respectively). Early stage was significantly more common in intestinal type than diffuse type gastric cancer (13.1%vs.0%; *P*-value = 0.02). 5-year survival rate of diffuse type and intestinal type gastric cancer patients were very grave(5.3% vs 9.4).

**Conclusion**: Patients with diffuse type was younger than intestinal type whereas early stage of diseases and anemia with anemic symptoms were commonly found in intestinal type gastric cancer. However, both histologic types of this particular cancer had very poor prognosis.

R. Vilaichone: None. T. Limprukkasem: None. V. Mahachai: None. P. Chotivitayatarakorn: None.

## P5.35 | Indicators of proliferation of gastric epithelial cells depend on the severity of atrophy in the gastric body among Caucasoids of Siberia

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**Introduction**: The specific mechanisms for the development of atrophic gastritis are still debated (Pimentel-Nunes P. et al., 2019).

**Aim**: To study the indices of apoptosis and proliferation of gastric epithelial cells in patients with corpus atrophic gastritis.

**Methods**: Clinical and endoscopic examination with sampling of biopsy specimens from the gastric mucosa was performed in 54 patients (31 men and 23 women) aged 45-60 years. The diagnosis of corpus gastritis was established on the basis of a modified Sydney system (Dixon M.F. et al., 1996). Proliferation markers (Ki-67 and PCNA) and apoptosis (bcl-2 and p53) were determined in biopsy specimens by immunohistochemistry.

**Results**: The indices of apoptosis (bcl-2 and p53) were not associated with atrophic gastritis. The indices of epithelial cells proliferation were lower in patients with atrophy compared with people with non-atrophic gastritis. Ki-67 was found in 5% of the cells in patients with atrophic gastritis and in 8% of the cells in patients with non-atrophic gastritis ($P < 0.001$). For PCNA these indicators were equal, respectively 4% and 9% ($P < 0.001$). As a result, regulatory ratios: proliferation/apoptosis rates were significantly higher in patients with non-atrophic gastritis compared with patients with atrophic gastritis. So Ki67/bcl2 index was 1.5 in patients with non-atrophic gastritis and 1.07 in patients with atrophic gastritis ($P < 0.001$); PCNA/bcl2 - 2.39 and 1.5, respectively ($P < 0.001$).

**Conclusion**: The data obtained suggests that the violation of proliferative-apoptotic relationships is more important for the development of corpus atrophic gastritis than just an increase in the indices of apoptosis.

V.V. Tsukanov: None. O.V. Peretyat'ko: None. A.S. Pulikov: None. A.V. Vasyutin: None. J.L. Tonkikh: None.

## P5.36 | Incidence of gastric cancer has been decreased with increased endoscopic resection of gastric adenoma; analysis of National Cancer Screening Program in Korea

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**Background/Aim**: The incidence of gastric cancer has been declining for the past decade. However, the cause has not been fully elucidated. The aim of this study was to evaluate the cause of declining tendency of gastric cancer in Korea.

**Methods**: We analyzed the data from National Cancer Screening Program (NCSP) and data from national Health Insurance, Review & Assessment (HIRA) Service. These data include over 98% of Korean population.

**Results**: Then number of endoscopic examination for screening gastric cancer has been markedly increased and endoscopic examination in clinical unit has been markedly decreased for the past decade. Increased detection of pathologically proven gastric adenoma has been found during this period. The number of endoscopic resection for gastric adenoma has been markedly increased, while the number of newly detected gastric adenocarcinoma has been decreased from 2011.

**Conclusions**: Endoscopic resection for gastric adenoma after detection by NCSP might be associated with declining tendency of gastric cancer in Korea. Most of gastric cancers follow the adenoma-carcinoma sequence in Korea.

B. Kim: None. S. Park: None. J. Kim: None. D. Cheung: None. J. Kim: None.

## P5.37 | Leading risk factors for gastric cancer in the population of Khakassia

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**Aim**: To analyze of risk factors of gastric cancer (GC) in patients of the Republic of Khakassia.

**Methods**: A retrospective study of cancer-register patients with GC of the Republic of Khakassia among period 2013-2017 was conducted. Consideration of risk factors for PU: gender, age of hospitalization; localization and type of cancer, HP status. Results. The incidence of GC in men was 55.2 ± 3.4%, in women - 44.8 ± 2.7% ($P = 0.002$). GC incidence rates per 100 thousand in men 14.4 ± 1.1% and in women 11.7 ± 1.2%, $P = 0.006$. The main age groups of GC patients: 50-59 years - 21.3%, 60-69 years - 28.38%, and 70-79 years - 26.17%. The critical age of the risk of GC is 50 years and older (for men it increases by 2 times, for women by 5.8 times). The leading localization are the body of the stomach is 30 ± 3.4%, the antral and pyloric sections are 22.1 ± 4.1%, the morphological type is adenocarcinoma (95.4 ± 2.3%). HP is highly infected: serological - 85%, morphological, rapid urease - more than 95%. Relatives of the first and second degree of kinship with GC were present in every fourth patient (23%), burdened heredity in cancer of a different location was confirmed in every second patient with GC (55%).Conclusion. Atrophic gastritis is a predictor of distal localization, hereditary burden, HP infection with an early history, realizing its potential through the Correa cascade, becomes the leading risk factor for carcinogenesis in the stomach at the age of 50 years or more, when the pool of patients increases exponentially.

E.S. Ageeva: None. O.V. Shtygasheva: None.

# POSTER ROUND 6.1 VIRULENCE FACTORS AND PATHOGENESIS OF HELICOBACTER INFECTION

## P6.01 | Role of non-canonical NF-κB signaling during *H. pylori*-induced inflammation and gastric carcinogenesis

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*Helicobacter pylori* has been described to activate non-canonical NF-κB pathway in the stomach during inflammatory conditions via lymphotoxin β receptor (LTβR) in a type IV secretion system (T4SS)-dependent manner. *H. pylori* uses different adhesion molecules and virulence factors to facilitate the infection of the stomach epithelium. Of those, HopQ has been shown to not only be involved in adhesion but also to interfere with the T4SS. Therefore, we aim at deciphering whether HopQ is involved in the activation of non-canonical NF-κB pathway. We infected gastric cancer cell lines with wild type or HopQ-deficient *H. pylori* strains and performed ELISA, qPCR and western blot to check for the activation of the pathway. Bacteria lacking HopQ induced less IL8 secretion, reduced *LTB*, *CXCL10* and *CCL2* mRNA expression compared to WT strains. In addition, HopQ was required for p100 to p52 processing. Further analysis is ongoing in order to determine whether CEACAM-HopQ interaction is involved in the activation of the non-canonical NF-κB pathway.

Additionally, we are further investigating whether activation of non-canonical NF-κB pathway is involved in gastric carcinogenesis. To this end, we generated a transgenic mouse model that specifically expresses lymphotoxin ($LT\alpha\beta^{TG}$), a specific ligand for LTβR, in the stomach under the control of the $H^+/K^+$ ATPase promoter. We infected these mice with a CagA-positive *H. pylori* strain to elucidate whether infection induces neoplastic changes in the stomach epithelium favouring gastric cancer development. Our results suggest an important role for non-canonical NF-κB pathway during *H. pylori*-induced inflammation, a predisposition for cancer development.

K. Taxauer: None. M. Gerhard: None. R. Mejías-Luque: None.

## P6.02 | Divalent metal ions differentially regulate *Helicobacter pylori* HtrA activity

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High temperature requirement A (HtrA) is a serine protease expressed by the human pathogen *Helicobacter pylori* (Hp). During infection HtrA is able to actively cleave the adherens junction protein and tumor suppressor E-Cadherin on gastric epithelial cells, which

induces disruption of the integrity of the gastric epithelium, thereby promoting Hp pathogenesis. Recent studies indicated that the presence of $Ca^{2+}$ blocked HtrA mediated E-Cadherin cleavage by interfering with the accessibility of the E-Cadherin $Ca^{2+}$-binding regions representing HtrA cleavage sites. Here, we investigated the influence of different divalent ions on the activity of HtrA.

In vitro cleavage experiments using HtrA and recombinant human E-Cadherin revealed a strong inhibitory effect of $Ca^{2+}$, $Zn^{2+}$ and $Cu^{2+}$ on HtrA mediated E-Cadherin cleavage. In casein degradation assays only $Zn^{2+}$ and $Cu^{2+}$ efficiently blocked HtrA activity. $Ni^{2+}$, $Co^{2+}$ and $Mn^{2+}$, on the other hand, increased the proteolytic activity of HtrA. Thermal shift assays indicated that $Zn^{2+}$ and $Cu^{2+}$ as well as $Ni^{2+}$ and $Co^{2+}$ bound to a newly identified metal-binding loop of HtrA in a concentration dependent manner. From these data, we concluded that $Ca^{2+}$ blocked E-Cadherin cleavage through binding to the E-Cadherin signature sites, while $Zn^{2+}$ and $Cu^{2+}$ exhibited direct inhibitory effects on HtrA. In conclusion we found that binding of divalent ions differentially affected the activity of Hp HtrA. These findings could contribute to the development of novel ion-dependent protease inhibitors which might provide a powerful new tool for combating *Hp* infections.

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## P6.03 | *Helicobacter pylori* inhibits GKN1 expression via the CagA /p-ERK/AUF1 pathway

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**Background**: Gastrokine1 (GKN1), an important tumour suppressor gene, is downregulated in *Helicobacter pylori* (HP) infected gastric mucosa and gastric cancer. However, the underlying mechanism of the downregulation of GKN1 in HP infection was not clearly elucidated.

**Methods**: We investigated whether GKN1 was downregulated during HP infection. The AUF1 gene was knockdown in gastric epithelial cells, we measured GKN1 expression to find their relationship. In addition, we conducted RNA-Protein Pull-Down and RNA-immunoprecipitation to judge whether AUF1 can bind GKN1. By measuring turnover and luciferase activity, we explored the GKN1mRNA stability while AUF1 was knockdown. During HP infection, we measured AUF1, GKN1 and p-ERK expression. We also observed the cell proliferation, migration, cell cycle when AUF1 was knockdown. Furthermore, during CagA knock-out HP infection, we measured the expression of AUF1, GKN1 and p-ERK.

**Results**: We suggested GKN1 was downregulated during HP infection and GKN1 was negatively correlated with AUF1. Further investigation revealed that AUF1 can decrease the GKN1mRNA stability by binding it. Moreover, We observed AUF1 was induced during HP infection and biological function studies demonstrated that AUF1 can promote cell proliferation, migration and accelerated G1/S phase transition. What's more, HP CagA can activate the p-ERK/AUF1/GKN1 pathway.

**Conclusion**: These data showed that HP CagA may promote gastric cancer tumorigenesis via p-ERK/AUF1/GKN1 pathway. The AUF1/GKN1 axis might serve as a prognostic biomarker as well as a novel potential target in the treatment of gastric cancer.

Y. guo: None. S. ding: None.

## P6.04 | Non-enzymatic properties of *Helicobacter pylori* urease

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Our group has been working with the urease of *Helicobacter pylori*(HPU) for almost 15 years. HPU has been considered an important *H. pylori* virulence factor since mutant strains with deleted urease lack the ability to colonize the human stomach. HPU is involved in several aspects of *H. pylori* pathogenesis, such as the activation of macrophages and their iNOS, the disruption of tight junctions, and the induction of immunological responses elicited by the enzyme and its subunits. Our work has focused on the unveiling of HPU's properties that do not require its enzymatic activity. HPU is capable of, in nanomolar concentrations, to induce eicosanoid-dependent platelet aggregation, activation of neutrophils while increasing their lifespan and eliciting production of reactive oxygen species, and activation of gastric epithelial and endothelial cells. The platelet-aggregating property of HPU relies on its B subunit in a GPVI-dependent manner, turning the platelets into a pro-inflammatory state, inducing the expression of IL-1βand CD14. HPU is internalized by gastric epithelial cells, upon which secreted pro-angiogenic factors. Angiogenesis by HPU was demonstrated both *in vitro* and *in vivo*, using HUVECs, HMECs and the chicken embryo chorioallantoic membrane assay. Moreover, our group showed that HPU drives endothelial cells into a ROS-dependent pro-inflammatory state, with enhanced angiogenic property which ultimately contributes to the progression of gastric carcinogenesis.

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## P6.05 | Role of CEACAM members 1 and 5 in type IV secretion of the effector protein CagA by *Helicobacter pylori*

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Prominent *H. pylori* virulence factors comprise the vacuolating cytotoxin VacA and the cagPAI-encoded type IV secretion system (T4SS). The T4SS effector protein CagA can be translocated into AGS and

other gastric epithelial cells to hijack signaling networks. The duodenal cell line AZ-521 has been recently introduced as novel model system to investigate CagA delivery and phosphorylation in a VacA-dependent fashion. In contrast, we discovered that AZ-521 cells display a T4SS incompetence phenotype for CagA injection, which represents the first reported gastrointestinal cell line with a remarkable T4SS defect. We proposed that this deficiency may be due to an imbalanced expression of the *H. pylori* receptors integrin-$\beta_1$ or carcinoembryonic antigen-related cell adhesion molecules (CEACAMs). We demonstrate that AZ-521 cells readily express integrin-$\beta_1$, but overexpression of integrin-$\beta_1$ constructs did not restore the T4SS defect. We further show that AZ-521 cells lack the expression of CEACAMs. We demonstrate that genetic introduction of either CEACAM1 or CEACAM5, but not CEACAM6, in AZ-521 cells is sufficient to permit injection of CagA by *H. pylori* to degrees observed in the AGS cell model. Expression of CEACAM1 or CEACAM5 in infected AZ-521 cells was also accompanied by tyrosine dephosphorylation of the cytoskeletal proteins vinculin and cortactin, a hallmark of infected AGS cells. Our results suggest the existence of an integrin-$\beta_1$- and CEACAM1- or CEACAM5-dependent T4SS delivery pathway for CagA, which is clearly independent of VacA. The presence of two essential host protein receptors during infection with *H. pylori* represents a unique feature in the bacterial T4SS world.

N. Tegtmeyer: None. S. Backert: None.

## P6.06 | *H. pylori* base-excision restriction enzyme: an oncoprotein?

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Which factor of *H. pylori* causes human genome instability in stomach cancer remains unknown. We found one family of restriction enzymes excise a base from its recognition sequence. They are DNA *N*-glycosylases as opposed to DNA phosphodiesterases (https://doi.org/10.1038/ncomms417). At the resulting abasic site (AP site), its uncoupled AP lyase activity may generate atypical strand breaks (https://doi.org/10.1093/nar/gkv116; https://doi.org/10.1093/nar/gkw1250). Cellular AP endonucleases can also introduce strand breakage at the AP site in a different way. Its members are present in Helicobacter (https://doi.org/10.1093/nar/gni113; https://doi.org/10.1093/nar/gkn718). Distribution of this (PabI) family in global *Helicobcter pylori* strains reflects ancient human migration (https://doi.org/10.1186/s12864-015-2021-3). We explored the possibility this enzyme acts on human genome. We found that chromosomal breakage in human cells after infection with *H. pylori* is decreased by mutational inactivation of this enzyme. Several other lines of evidence also support our hypothesis that this base-excision restriction enzyme acts on human genome and causes stomach cancer.

I. Kobayashi: None. K. Hanada: None. M. Fukuyo: None. K. Yahara: None. H. Yonezawa: None. &. Venclovas: None. Y. Katsura: None. A. Toyoda: None. S. Nishiumi: None. T. Azuma: None. M. Kato: None.

## P6.07 | *Helicobacter pylori* outer membrane vesicles induce expression of ICAM-1 via a GILZ, MAPK-, NF-kB-dependent pathway in endothelial cells

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*H. pylori* shed outer membrane vesicles (OMVs) that contain many of the surface elements of the bacteria. Although *H. pylori*-derived OMVs may contribute to the pathogenesis of *H. pylori* infection, responses of endothelial cells (ECs) to OMVs have not been elucidated. In the present study, we investigated whether *H. pylori* OMVs affected the expression of intercellular cell adhesion molecule (ICAM)-1 and monocytic adhesion to endothelial cells (ECs). Exposure of human umbilical vein ECs (HUVECs) with *H. pylori* OMVs resulted in the induction of ICAM-1 expression. OMVs obtained from a cagA-negative isogenic mutant strain induced less ICAM-1 expression than OMVs obtained from a wild-type strain. In addition, OMVs induced the activation of IκB kinase (IKK) and NF-κB signals. Suppression of IKK and NF-κB activity in ECs significantly reduced ICAM-1 expression and adhesion of monocytes to ECs. Moreover, inhibition of p38 significantly attenuated the OMV-induced ICAM-1 expression in ECs. Furthermore, suppression of glucocorticoid-induced leucine zipper (GILZ) resulted in the inhibition of monocyte adhesion to HUVECs. These results suggest that a signaling pathway involving GILZ, p38 MAPK, IKK, and NF-κB is required for ICAM-1 induction in ECs exposed to *H. pylori* OMVs, and may be involved in the leukocyte-adhesion cascade following *H. pylori* infection.

J. Kim: None.

## P6.08 | *Helicobacter pylori* invades human gastric mucosa, up to perforate and go through the basal membrane: Evidence due to an ultrastructural study

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**Background**: The interaction between *Helicobacter pylori* (Hp) and gastric mucosa leads to: Hp adhesion, formation of Type IV Secretion

System "pili" that inject CagA into mucous cells cytoplasm, tight junction's disruption and cell death.

We previously investigated the related ultrastructural aspects. Dobois and Boren (2007), observing silver -stained histological sections, found Hp on mucosal surface, in lamina propria inflammatory cells, and in post-capillary venules, even attached to erythrocytes.

**Aim**: To study Hp intra-cellular and extra-cellular pathways by electron microscopy.

**Material and methods**: A retrospective study was performed on 300 SEM/TEM micrographs taken from 109 human gastric biopsies that we processed using our technique to compare Light, Transmission (TEM) and Scanning Electron Microscopy (SEM) observations in the same specimen.

**Results**: *TEM*: 1-Hp was rarely found intact within mucous cells; 2-more epithelial cells show phagolysosomes containing the residues of bacterial digestion; even fragments of bacteria are recognizable.

*SEM*: Hp passes through cell junctional complex and perforates the basal membrane; holes are quite evident in which Hp penetrates; the bacteria appear definitely vital, even if deprived of flagella; in fact they show binary fission.

**Conclusions**: Hp escapes host innate defence, being phagocytosis ineffective; it survives crossing the gastric mucosal barrier and takes contact with capillary circulation; Researches are in progress to correlate Hp virulence with host blood group and severity of systemic associated diseases**.**

F. Bonvicini: None. T. Dionisi: None. A. Gasbarrini: None. G. Gasbarrini: None.

## P6.09 | *Helicobacter pylori* outer membrane protein genes expression in gastric biopsy specimens of patients and their association with clinical, endoscopic and histopathologic findings

D. Davoudi Oskouei[1]; H. Akpınar[2]; S. Sarioğlu[3]; P. Keskinoğlu[4]; M. Soytürk[2]; H. Ellidokuz[4]; &. Şimşek[2]; **Ö. Yılmaz**[1]

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**Objective**: To investigate the expression of *Helicobacter pylori* outer membrane protein plus *cagA* genes in gastric biopsy specimens of patients by real-time reverse transcription PCR (RT RT-PCR) and their association with clinical, endoscopic and histopathologic findings.

**Methods**: Gastric antral and corporal *biopsies* from 120 patients were studied by rapid urease test (RUT), histopathology and culture. Gastric biopsies from 101 patients were examined for the expression of *H. pylori* cagA, omp6, omp13 (oipA), omp18, omp20 genes by RT RT-PCR. The results were evaluated and statistically analyzed between patients with different clinical, endoscopic and histopathologic findings.

**Results**: *H. pylori infection* was *determined* based on both positive RUT and histopathology. RT RT-PCR was positive in 77 of 101 patients. Gene expression frequencies of *cagA*, *omp6*, *omp13*, *omp18*, *omp20* in the antrum and corpus together of 45 patients with *H. pylori infection* were 30(66.7%),35(77.8%),37(82.2%),45(100.0% ),37(82.2%) respectively. Endoscopic findings of 48 patients were gastric ulcer/erosion(n = 6), duodenal ulcer/erosion(n = 6), erosive gastritis(n = 11) and non-erosive gastritis(n = 25).The Expression frequencies of five studied genes were not associated with endoscopic findings ($P > 0.05$). Only the level (ΔCt) of *omp13* gene expression was found to be statistically significant ($P = 0.005$) between patients with gastric ulcer/erosion and non-erosive gastritis. *H. pylori* infection was associated with infiltration of polymorphonuclear and mononuclear leukocytes (PNL, MNL) as well as *H. pylori density* in the antrum and corpus but not associated with intestinal metaplasia (IM). There were not found any associations between the gene expression frequencies/levels and *H. pylori density*, PNL, MNL($P > 0.05$).

**Conclusion**: *omp13* which encodes an important inflammatory protein might play role in the pathogenesis of *H. pylori* infection.

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## P6.10 | Phylogenetic and genetic polymorphism analysis of oipA, babA, sabA and homB gene of *Helicobacter pylori* strains from Chinese patients with different diseases

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**Aims**: The outer membrane proteins (OMPs) of *Helicobacter pylori* (*H. pylori*) are important virulence factors in the attachment and colonization of gastric epithelial cells. The aim of this study was to perform phylogenetic and genetic polymorphism analysis of four OMPs of clinical *H. pylori* strains from different gastric diseases.

**Methods**: Genomic DNA of 177 clinical *H. pylori* isolates were extracted and genotypes of oipA, babA, sabA, and homB gene were performed. Functional switch status of oipA and sabA genes were analysed. In addition, phylogenomic analysis with 30 reference strains from the NCBI were performed with MEGA X software. Genetic polymorphism and positive selection analysis were conducted by DnaSP6.0 software.

**Results**: The prevalence of oipA, babA, sabA and homB gene were observed 100%, 92.7%, 94.3% and 96.0%, respectively. 98.3% and 76.3% of strains had functional status of oipA and sabA gene. Interestingly, both of the two gene showed a different functional status independent of phase change. Phylogenetic analysis showed four genes of *H. pylori*

from different diseases mainly clustered with HpAsia clades and were widely grouped into different clades. The average nucleotide diversity of oipA, babA, sabA and homB gene from different diseases were 0.023, 0.065, 0.107 and 0.081 with positive selection.

**Conclusions**: oipA, babA, sabA and homB gene of *H. pylori* are highly prevalent and diverse, but no significant association with the clinical outcomes or histopathological changes was found among patients in China. The four OMPs are geographically distributed and under positive selection, among which sabA gene is the most highly genetic polymorphism.

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## P6.11 | *Helicobacter pylori*-induced DNA damage is a potential driver for human gastric cancer AGS cells

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**Aims**: *Helicobacter pylori* (*H. pylori*) is a major cause of gastric cancer. This study was aimed to explore the characteristic of DNA damage induced by *H. pylori* infection in gastric cancer AGS cells.

**Results**: After infection with *H. pylori*, the ROS levels in AGS cells were significantly higher than those in the uninfected cells. Cells with longer comet tails were detected after infection with *H. pylori*. The number of APE1- and γH2AX-positive cells was significantly increased compared to the number of negative control cells. The expression of pChk1 and pChk2 was significantly upregulated by *H. pylori* infection. Cell growth was inhibited after *H. pylori* infection. All these results were dose-dependent. The cell alterations were more significant upon infection with *H. pylori* at an MOI of 100:1 than at an MOI of 50:1.

**Conclusions**: *H. pylori* infection can induce DNA single-strand breaks, DNA double-strand breaks and cell cycle checkpoint activation following ROS generation in the gastric cancer cell line AGS, which is a potential driver for gastric cancer.

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## P6.12 | *Helicobacter pylori*, gastroesophageal reflux disease (GERD) and gastritis in children

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The role of *H. pylori* in gastritis development had been proved, but at the same time GERD is not discussed.

**Aim of the research**: To study *H. pylori* in GERD children with different activity of gastritis and association of these diseases with bacterial invasion.

**Material and Methods**: We examined 309 schoolchildren with gastroenterological complains in the ages from 7 to 17 years. GERD diagnostics was made in accordance with Montreal consensus (Vakil N. et al., 2006). All of them were performed gastroscopy with biopsy sampling from stomach antrum and body. *H. pylori* identification was carried out by morphological method after Gimza coloring. Gastritis was estimated according to Sydney classification. The analysis of statistical meanings of the differences between qualitative characteristics was made by $\chi^2$ criterion, under <0.05.

Results: *H. pylori* in GERD children was revealed in 59.2% (without GERD - 57.3%, $P = 0.8074$). Bacterial invasion indices in children with the activation of antrum gastritis of 2-3 stages - 79.9%, 1 stage - 36.9% ($P = 0.0001$); body stomach gastritis of 2-3 stages of activity - 71.7%, of 1 stage - 51.6% ($P = 0.0011$).

In the infected children with antral gastritis of 2-3 stages of activity, GERD was diagnosed in 21.0%, of 1 stage in 6.8% ($P = 0.0155$). In *H. pylori* children with stomach body gastritis of 2-3 stages of activity we marked GERD in 16.7%, on 1 stage of activity in 16.1% ($P = 0.9173$).

**Conclusion**: We have found the association of GERD with the activity of inflammation in stomach antrum in *H. pylori* children.

V.A. Vshivkov: None. T.V. Polivanova: None. V.V. Tsukanov: None.

## P6.13 | The cagA and some outer membrane proteins gene expression profiles in gastric tissues of adult Turkish patients with *Helicobacter pylori* infection

D. Davoudi Oskouei[1]; H. Akpınar[2]; S. Sarioğlu[3]; P. Keskinoğlu[4]; H. Ellidokuz[4]; M. Soytürk[2]; &. Şimşek[2]; **Ö. Yılmaz**[1]

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**Objective**: *Helicobacter pylori* is highly pleomorphic bacterium. *Heterogeneity among H. pylori strains in* expression of the CagA as well as OMPs is thought to be important in determining *clinical outcome of patients* with *H. pylori* infection. HP-OMP-genes like omp13(oipA) and omp18 play a role in inflammation while omp6 and omp20 are involved in the bacterial-host interactions. Real-time reverse transcription PCR(RT RT-PCR) was used to study the frequencies and levels of the expression HP-*cagA* and OMP-genes in patients with HP-infection in association with endoscopic and histopathologic findings.

**Methods**: Gastric antral and corporal *biopsies* from 120 patients were studied by RUT and histopathology. Culture was performed on gastric biopsies of 104 patients. Gastric biopsies from 101 patients were examined for gene expressions of HP-*cagA* and OMPs (*omp6*, *omp13*, *omp18*, *omp20*)with *ureA* and 16S-rRNA house-keeping genes by RT RT-PCR. Total RNA from each-antrum and-corpus was

extracted and cDNA was synthesized to determine HP-*cagA* and OMP-genes expression status.

**Results**: 48/120 patients(40.0%) were positive for HP-infection by RUT and histopathology. 30/48 patients(85.7%)were culture positive. RT RT-PCR was positive in 45/48 patients (93.8%)with HP-infection. *cagA* gene expression was positive in gastric biopsies of 30/45 patients(66.7%).This rate was lower than those of *omp6*, *omp13*, *omp20* genes which were 35(77.8%),37(82.2%),37(82.2%) respectively. *omp18* was expressed in gastric biopsies of 45 patients(100.0%). Expression frequencies of studied genes were not statistically associated with endoscopic or histopathologic findings($P > 0.05$).The mean Ct values of these genes in antrum were lower than those of corpus. The *omp6* gene expression level in corpus was higher than in antrum.

**Conclusion**: The positive expression of either *cagA* or OMP-genes did *not have* a statistically significant *impact* on *patients' clinical outcome in our hospital.*

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## P6.14 | Identification of anti East Asian CagA specific antibody in *Helicobacter pylori* strains of Turkish Origin

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**Background**: Several studies indicated that *Helicobacter pylori* strains which had variable *cag*A gene are associated with higher risk of diseases. The *cagA* gene has two different allele types: the western allele(EPIYAC)and the east-Asian alleles (EPIYAD).The goal of the present study was to identify CagA EPIYA motifs and East-Asian alleles (EPIYAD) by anti East Asian CagA specific antibody with immunohistochemical method in *H. pylori* strains of Turkish origin.

**Method**: Antrum and corpus biopsies obtained for histology, rapid urease test, and culture by endoscopy performed in 193 patients (M:F = 56:137).Paraffin embedded-gastric biopsy tissue sections of all cases were studied by immunohistochemistry(IHC) method and were examined for anti East Asian CagA specific(aEAS) antibody. *cag*A genotypes were also examined from isolated DNA from *H. pylori* strains by PCR and EPIYA motifs were determined by DNA sequencing.

**Result**: *H. pylori* was positive in 73.1%(141/193).Among the *H. pylori* positive 141 cases, 119 cases were positive for IHC with a *H. pylori* antibody. All *H. pylori* positive cases of IHC were examined for a CagA antibody: 76 cases(63.9%) were positive. In those 76 cases of CagA positive, IHC with a EAS antibody positive was one case(1.3%).CagA was analyzed by PCR and IHC with a CagA antibody. Both two tests were positive and negative were 41 cases and 106 cases, respectively. Positive for PCR but negative for IHC with a CagA antibody was eight cases. Positive for IHC with a CagA antibody but negative for PCR was 35 cases. Among 30 *cag*A positive strains; 21(70%) had EPIYA ABC, seven(23.3%) had EPIYAABCC and in two patients(6.7%) had both EPIYA ABC and ABCC. No cases were positive in culture positive patients but one patient was positive by antiEast Asian CagA specific antibody.

**Conclusion**: *H. pylori* was positive in 73.1%(141/193) and high virulent East Asian CagA positive *H. pylori* rate is low in Turkish population.

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## P6.15 | Genetic feature of *H. pylori* in children with chronic gastritis and atopic dermatitis

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**Background**: Researchers ' data on the relationship of *H. pylori* (HP) and atopic diseases in children are contradictory. Genetic features of HP in combination of chronic gastritis (CG) and atopic dermatitis (AtD) are insufficiently studied.

**The aim**: To carry out a comparative assessment of molecular genetic features of HP in children with CG and concomitant AtD and in patients with CG without atopy.

**Methods**: 52 patients (10 to 17 years) with diagnosis of CG and HP were examined. Patients were divided into groups: (1) children with atopic dermatitis - AtD and CG (26 people); (2) children with chronic gastritis - CG (26 people). Specific genomic sequences of HP virulence factors were identified: UreC, CagA, CagC, CagH, CagE. by PCR in real time using a set of reagents.

**Results**: In patients with HP-associated CG and AtD, the presence of genes of HP ureC virulence factors (84.62% and 57.69%, $P < 0.01$), CagE (65.38% and 46.15%, $P < 0.01$) was significantly more often revealed. In the CG group without atopic dermatitis were significantly more often identified the presence of CagA (65.38% and 84.62%, $P < 0.05$). Differences in the presence of CagC, CagH between groups we have not received.

**Conclusion**: In children with HP-associated gastritis, and atopic dermatitis was significantly more frequent in the presence of the genes of virulence factors of HP: the Cag UreC and E a more rare occurrence of CagA. The Role of virulence genes in development requires further investigation.

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## P6.16 | Genetic diversity of 3′ Region of the *cagA* gene in *Helicobacter pylori* isolates from individual patients

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**Introduction**: *H. pylori* shows extraordinary genetic diversity between different patients as well as in a single patient.*cagA* gene is a *H. pylori* virulence factor that poses genetic diversity in isolates from different patients. In this study, variability of 3′ region of the *cagA* gene was studied in *H. pylori* isolates from individual patients.

**Methods**: In 14 *H. pylori*- positive patient, four single colonies were isolated from the primary *H. pylori* culture plates. *cagA* status and genotype of variable 3′ region of the *cagA* gene was determined by PCR amplification using appropriate primers.

**Result**: In 11/14 patients, all four isolates were *cag* $A^+$. variation in 3′ region of *cagA* (type A: 642 bp, B: 756 bp and C: 810 bp) was observed in 6/11 patients (Table). In 3/14 patients the *cagA* genotype are as follows; patient 1: two $cagA^+$ with variation (type B and C) and 2 $cagA^-$, patient 2: two $cagA^+$ without variation and 2 $cagA^-$ and patient 3: one $cagA^+$ and 3 $cagA^-$.

| | Patient 1 | | | | Patient 2 | | | | Patient 3 | | | | Patient 4 | | | | Patient 5 | | | | Patient 6 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Isolates** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** | **1** | **2** | **3** | **4** |
| Strain type | C | B | B | C | A | A | A | B | A | C | B | C | A | A | B | B | C | B | B | B | C | C | A | A |

**Discussion**: Results of this study showed that different *cagA* variants may be simultaneously present in the same stomach. Further studies will determine any correlation between *cagA* genetic diversity and clinical outcomes of *H. pylori*.

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## P6.17 | Allelic diversity of *H. pylori vacA* gene within the gastric niche of individual patients

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**Introduction**: *Helicobacter pylori* isolates harvested from different individuals are highly polymorphic. Strain variation also has been observed within a single host. In this study diversity of *H. pylori* vacA gene (s and m) was evaluated within 12 dyspeptic patients

**Methods**: Gastric biopsies from 12 *H. pylori*-positive patients were cultured on selective brucella blood agar and incubated microaerobically for 5-7 days. Four single colonies per patient were picked from the primary *H. pylori* culture plates and sub-cultured to obtain pure *H. pylori* isolates. All *H. pylori* isolates were further analyzed by amplification of *vacA* alleles (s and m) by PCR.

**Results**: From 12 recruited patients, nine patients had *H. pylori* isolates with different *vacA* genotype (table 1). No variation was found in remaining three patients (patient 1: s1m2, patient 2: s2m2 and patient 3: s2m1).

| | Patient 1 | | | | Patient 2 | | | | Patient 3 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Isolates | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| vacA genotype | s2m1 | s2m2 | s2m2 | s2m2 | s2m2 | s2m2 | s1m1 | s1m1 | S1m1 | S1m1 | S2m1 | S1m1 |
| | **Patient 4** | | | | **Patient 5** | | | | **Patient 6** | | | |
| Isolates | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| vacA genotype | S2m2 | S2m2 | S2m2 | S1m1 | S2m2 | S1m1 | S1m1 | S2m2 | S2m1 | S1m1 | S1m1 | S1m1 |
| | **Patient 7** | | | | **Patient 8** | | | | **Patient 9** | | | |
| Isolates | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| vacA genotype | S1m2 | S1m1 | S2m1 | S1m2 | S2m1 | S1m1 | S1m1 | S1m1 | S2m1 | S2m1 | S2m1 | S2m2 |

**Discussion**: Results of this study showed that *H. pylori* population with different genotypes may colonize in the stomach of single host. Accordingly, co-existence of diverse genotypes of putative virulence factors in a single host

must be considered when drawing a correlation with clinical presentation.

P. Saniee: None. M. Raoofimanesh: None. F. Siavoshi: None. S. Kadkhodaee: None. G. Poostizadeh: None.

## P6.18 | Antibiotic resistance and genotypes of *Helicobacter pylori* strains in patients with gastroduodenal disease in south-east Poland

**I. Korona-GloWniak**; H. Cichoz-Lach; R. Siwiec; S. Andrzejczuk; A. Malm

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Genetic diversity of virulence genes of *H. pylori*, which is geographically and ethnically structured, play an important role in the pathogenesis of gastrointestinal disease. The aim of this study was to investigate the importance of virulence markers to predict clinical outcome as well as to determine an antibiotic susceptibility of *H. pylori* strains isolated in Poland. Gastric biopsies from 132 patients with gastrointestinal disorders were tested for presence of *H. pylori* with the use of rapid urease test, microbial culture and polymerase chain reaction (PCR) detection. The genetic diversity of 62 *H. pylori* positive samples was evaluated by detection of *cagA* and PCR-typing of *vacA* and *iceA* virulence-associated genes. Thirty five *H. pylori* strains were cultured from gastric biopsy samples and their antibiotic susceptibility were tested by E-test method. PCR was the most sensitive and specific method of *H. pylori* detection in gastric biopsies (56.5%). The most common *H. pylori* genotypes infecting the studied patients were *cagA(+)vacAs1m2* (27.4%), *cagA(-)vacAs2m2* (24.2%) and *cagA(+) vacAs1m1* (19.4%). Among 35 of cultured *H. pylori* strains, 51% were susceptible to all and 49% were resistant to at least one of the tested antibiotics.

**Conclusion**: This is the first study that reports the high incidence and diversity of allelic combination of *cagA*, *vacA* and *icaA* genes in gastroduodenitis patients in Poland. Genotyping of *H. pylori* strains confirmed the involvement of *cagA* gene and *vacA s1m1* genotype in development and severity of gastric disorder.

I. Korona-Glowniak: None. H. Cichoz-Lach: None. R. Siwiec: None. S. Andrzejczuk: None. A. Malm: None.

## P6.19 | Western-Type *Helicobacter pylori* CagA are the Most Frequent Type in Mongolian Patients

**T. Tserentogtokh**[1,2]; B. Gantuya[1,3]; P. Subsomwong[3]; K. Oyuntsetseg[1]; D. Bolor[4]; Y. Erdene-Ochir[5]; A. Azzaya[3]; D. Davaador[1]; T. Uchida[6]; T. Matsuhisa[7]; Y. Yamaoka[3,8,9]

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*Helicobacter pylori* infection possessing East-Asian-type CagA is associated with carcinogenesis. Mongolia has the highest mortality rate from gastric cancer. Therefore, we evaluated the CagA status in the Mongolian population. High risk and gastric cancer patients were determined using endoscopy and histological examination. *H. pylori* strains were isolated from different locations in Mongolia. The CagA subtypes (East-Asian-type or Western-type, based on sequencing of Glu-Pro-Ile-Tyr-Ala (EPIYA) segments) and vacA genotypes (s and m regions) were determined using PCR-based sequencing and PCR, respectively. In total, 368 patients were examined (341 gastritis, 10 peptic ulcer, and 17 gastric cancer). Sixty-two (16.8%) strains were cagA-negative and 306 (83.1%) were cagA-positive (293 Western-type, 12 East-Asian-type, and one hybrid type). All cagA-negative strains were isolated from gastritis patients. In the gastritis group, 78.6% (268/341) had Western-type CagA, 2.9% (10/341) had East-Asian-type, and 18.2% (61/341) were cagA-negative. However, all *H. pylori* from gastric cancer patients possessed Western-type CagA. Histological analyses showed that East-Asian-type CagA was the most virulent strains, followed by Western-type and cagA-negative strains. This finding agreed with the current consensus. CagA-positive strains were the most virulent type. However, the fact that different CagA types can explain the high incidence of gastric cancer might be inapplicable in Mongolia.

T. Tserentogtokh: None. B. Gantuya: None. P. Subsomwong: None. K. Oyuntsetseg: None. D. Bolor: None. Y. Erdene-Ochir: None. A. Azzaya: None. D. Davaador: None. T. Uchida: None. T. Matsuhisa: None. Y. Yamaoka: None.

## POSTER ROUND 6.2 INFLAMMATION, IMMUNITY, VACCINES AND HOST INTERACTION

### P6.20 | Identification of the functional role of the bacterial effector and oncoprotein CagA expressed by *Helicobacter pylori* in immune cells

**B. E. Chichirau**; S. Diechler; T. Scheidt; A. Benedetti; C. Freinek; G. Posselt; S. Wessler

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Expression of CagA (cytotoxin associated gene A), a virulence factor of *Helicobacter pylori* (*Hp*) is strongly connected to the development of gastric diseases and MALT lymphoma. CagA is injected into the cytoplasm of epithelial cells, where it is phosphorylated at the tyrosine residues of the EPIYA motifs. Translocation of CagA also occurs in B cells, however the signal transduction pathways regulated by this protein are not well defined. Here, we investigated the role of CagA on B cells proliferation, apoptosis and differentiation in infection experiments using ΔcagA and cagA positive *Hp* strains. The successful translocation of CagA in immune cells has been confirmed via western blot analysis by the presence of phosphorylated CagA. The bacterial adherence to the gastric epithelial cells did not vary significantly amongst the two strains, as observed in CFU assays. B cell viability was assessed through MTT analyses which revealed that short term infections with the cagA positive strain led to an increase of the cell proliferation rate, whereas the long term ones presented an opposite effect. mRNA expression analyses performed with both infected and uninfected samples showed an up- and down-regulation of several genes involved in NFkB mediated inflammatory response, in cellular death and survival by interfering with Akt and Erk1/2 pathways and in the regulation of immune cell trafficking. Immunofluorescence and B cell activation assays will be further conducted for identifying the impact of CagA on B cell regulation. Moreover, the possibility of using these bacterial strains in mouse model infections will be investigated.

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### P6.21 | The association between *Helicobacter pylori* infection and the immune response to CVD 103-HgR live oral cholera vaccine

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**Background**: *Helicobacter pylori* infection is suspected to affect the immune response to oral enteric vaccines; however, the nature and magnitude of effects are unclear.

**Objective**: To examine the association of *H. pylori* sero-prevalence and serum pepsinogens (PGs), as markers of gastric inflammation, with the immune response to a live oral cholera vaccine CVD 103-HgR (PXVX0200) among Malian adults.

**Methods**: A sero-epidemiological study was conducted utilizing sera of Malian adults who were vaccinated with cholera vaccine CVD 103-HgR in the framework of phase II clinical trial. Healthy adults, aged 18-45 years received a single oral dose of ≥ $2x10^8$ CFU (low dose, n = 48) of CVD 103-HgR or ≥ $2x10^9$ CFU of CVD 103-HgR (high dose, n = 49). Sera were tested for the presence of *H. pylori* IgG antibodies and concentrations of serum PGI and PGII by ELISA. The outcome variable, vibriocidal antibody seroconversion was defined as 4-fold increase in vibriocidal titers 14-days after immunization compared to baseline level.

**Results**: *H. pylori* IgG sero-positivity was 80%. *H. pylori* positive vaccines had higher PGII levels and lower PGI:PGII ratio than negative ones ($P$ = 0.02). Vibriocidal antibody seroconversion was higher among *H. pylori* sero-positive persons than negative ones: 64% vs 26%, $P$ = 0.004. This positive association was maintained in multiple regression model: adjusted prevalence ratio: 2.31 (95% CI 1.07-5.05), $P$ = 0.034. No significant associations were found between PG levels and vibriocidal seroconversion.

**Conclusions**: A better immune response to oral cholera vaccine CVD 103-HgR was found among *H. pylori* sero-positive adults than negative ones in Mali.

K. Muhsen: None. S.O. Sow: None. M.D. Tapia: None. M. Reymann: None. M.F. Pasetti: None. M.M. Levine: None.

### P6.22 | Walnut extracts inhibit *Helicobacter pylori*-induced stat3 tyr705 phosphorylation through activation of SOCS1 initiated with PPAR-gamma

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The health beneficial effects of walnut extract plentiful of n-3 poly-unsaturated fatty acid had been attributed to its anti-inflammatory

and anti-oxidative properties against various clinical diseases. Since we have published Fat-1 transgenic mice overexpressing *3-desaturase* significantly mitigated *H. pylori*-associated gastric pathologies including rejuvenation of chronic atrophic gastritis and prevention of gastric cancer, in this study, we have explored the underlying molecular mechanisms of walnut extracts against *H. pylori* infection. Fresh walnut phenolic extracts (WPE) were found to suppress the phosphorylation and nuclear translocation of signal transducer and activator of transcription 3 (STAT3) induced by *H. pylori* infection in RGM-1 normal gastric mucosal cells. Notably, *H. pylori* infection significantly decreased suppressor of cytokine signaling 1 (SOCS1), but WPE induced expression of SOCS1, Knockdown of SOCS3 abolished the suppressive effect of walnut extracts on STAT3 Tyr705 phosphorylation induced 1 by *H. pylori* infection. WPE induced nuclear translocation, DNA binding, and transcriptional activities of peroxisome proliferator-activated receptor gamma (PPARγ) in RGM1 cells. Knockdown of PPARγ inhibited the transcription of SOCS1 and attenuated the suppressive effect of WPE on phosphorylation of STAT3 Tyr705 induced by *H. pylori*. In addition, WPE inhibited the expression of c-Myc and IL-6/IL-6 signaling, which was attenuated in the RGM1 cells harboring SOCS1 specific siRNA. Conclusively, WPE inhibits *H. pylori*-induced STAT3 phosphorylation in a PPARγ and SOCS1-dependent manner.

K. hahm: None. Y. Shin: None.

## P6.23 | Interaction of *Helicobacter pylori* with Toll-Like receptors: role in infection control and resolution of inflammation

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*Helicobacter pylori*is a paradigm of persistent infections and chronic inflammation. The early detection of *H. pylori* by Toll-like receptors (TLRs) and other pattern recognition receptors is believed to induce a regulatory cytokine and chemokine profile that eventually blocks the resolution of inflammation. *H. pylori* factors such as HSP-60, NapA, DNA, and RNA are reported to be recognized by specific TLRs. However, *H. pylori* flagellin evades the recognition of TLR5 and LPS exhibits a low intrinsic activity on TLR4. Using HEK293 reporter cells expressing individual TLR members, we demonstrate that *H. pylori* can activate TLR2, TLR4, TLR5, TLR9 and TLR10, while TLR-negative HEK293 control cells only secreted cytokines in small amounts, in agreement with *cag*PAI functions being absent in this cell model. In contrast, HEK293-TLR cells were highly competent for inducing the secretion of IL-8, TNFα and other cytokines. Using phospho-specific antibodies and luciferase reporter assays, we further demonstrate that *H. pylori* induces IRAK-1 and IκB phosphorylation in a TLR-dependent manner, required for activation of transcription factor NF-κB. Finally, NF-κB activation was confirmed by p65-GFP translocation from the cytoplasm into the nucleus. We further evaluated the expression of novel nuclear targets by TLR signaling using whole genome cDNA microarrays. We identified various signal transduction events leading to the production of pro- and anti-inflammatory mediators through activation of NF-κB, MAP kinases, and IRF signaling pathways. Hence, the interplay of TLRs and *H. pylori* factors highlight the complexity of innate immune recognition and immune evasion as well as progression of gastric pathology.

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## P6.24 | Generation of a recombinant *H. pylori* UreB-*L. casei* strain and evaluation of its immunogenic and protective efficacy in mice

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**Background**: A safe and effective vaccine against *Helicobacter pylori*(Hp)is in high demand. Here, we have generated a recombinant *H. pylori* UreB-*Lactobacillus casei* (Lc) strain and evaluated the resulting antigen-specific immune responses and protective efficacy, in a mouse model.

**Methods**: Recombinant UreB (rUreB) was cloned and expressed in *E. coli*. For the construction of recombinant Lc, the *pgsA-ureB* sequence was synthesized and cloned into pNZ7021 plasmid. The sequence-confirmed recombinant pNZ7021-pgsA-UreB was transformed into Lc, by electroporation. Mice were immunized with wild-type and recombinant UreB-Lc (rLc), with/without rUreB and evaluated for their induced antigen-specific immune responses and protective efficacy, against live Hp challenge.

**Results**: Construction of the pNZ7021-pgsA-*ureB* was confirmed by enzymatic digestion and sequencing. Following immunization, serum anti-UreB IgG and IgA were significantly higher in all immunized groups, vs controls ($P < 0.05$), except for the wild-type Lc-only group. Amongst the former groups, those having received rLc had significantly higher serum anti-UreB IgG and IgA, than the wild-type ($P < 0.0001$). Hp challenge boosted serum IgG responses in the wild-type ($P < 0.0001$) and rLc, plus rUreB ($P < 0.01$) groups. Serum IgA responses, however, were only boosted in the rLc groups, regardless of the presence of rUreB ($P < 0.05$). According to the RUT and Hp qPCR analysis, all immunization (including wild-type and rLc with/without rUreB) regimens were protective, similar to that of the positive (CT + rUreB) control group.

**Conclusion**: These observations suggest the endogenous production of UreB, in our rLc strain and provide support for the antagonistic/adjuvant effects of wild-type Lc, in the Hp mouse model.

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## P6.25 | Vaccine failure against *Helicobacter pylori* explained by Cgt-dependent cholesterol depletion

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*H. pylori* is chemotactically attracted by host cell cholesterol, which led us to the identification of an enzyme globally present in *H. pylori*, cholesterol glucosyl transferase (Cgt). Cgt modifies host cell cholesterol and thereby extracts it from host epithelial membranes in order to incorporate the modified form into its own outer membrane (Wunder 2006; Lebrun 2006). Feeding infected mice with a cholesterol-rich diet leads to an increased inflammatory score characterized by upregulation of interferon-related pathways, reducing *H. pylori* colonization. We have recently succeeded with explaining the molecular context of these complex phenomena. Accordingly, Cgt-mediated depletion of cholesterol from epithelial cells during *H. pylori* infection causes downregulation of interferon-related signaling routes. This is due to the disruption of lipid rafts in host cell membranes, which prevents the activation of IFNG and IL-22 receptors (Morey 2018). Cholesterol depletion thus causes a complete block of immune effector signaling induced by infiltrating activated immune cells. Consequently, immune cells generated in the course of infection or by vaccination are not able to instruct the epithelium to exert its protective function against *H. pylori*, e.g. via the release of antimicrobial peptides. Rather, we propose that excessive stimulation of T-cell function by vaccination is likely to lead to a non-productive inflammatory phenotype with little effect on the elimination of *H. pylori* (Meyer & Morey 2019).

T. Meyer: None.

## P6.26 | High concordance rates of premalignant gastric lessions assessed by OLGA and OLGIM in monozygotic and dyzigotic twins

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**Background**: The development and progression of chronic *H. pylori* gastritis toward pre-neoplastic gastric lesions is a multifactorial process. To date, there are no studies that would evaluate the role of shared genetic influences on susceptibility and phenotype of chronic *H. pylori* gastritis and premalignant gastric alterations in twins. Aims: To compare histological alterations of gastric mucosa according to Sydney classification, OLGA and OLGIM staging systems in monozygotic and dizygotic twins.

**Methods**: This prospective study included 13 pairs of monozygotic and 16 pairs of dizygotic twins aged >18 years. At endoscopy five gastric biopsy specimens were collected according Sydney System protocol. *H. pylori* gastritis was assessed by histology and graded by OLGA and OLGIM staging systems.

**Results**: Concordance rate for chronic *H. pylori* gastritis in monozygotic twins was 69.2% and in dizygotic twins 62.5%, $P > 0.05$. Concordance for antrum athrophy in monozygotic twins was 76.9% and 75% in dizygotic twins ($P > 0.05$). Concordance for corpus athrophy in monozygotic twins was 92.3% and in dizygotic twins 87.5% ($P > 0.05$). Concordance for antrum IM in monozygotic twins was 84.6% and in dizygotic 75% ($P > 0.05$). Concordance for corpus IM in monozygotic twins was 84.6% and in dizygotic 93.7% ($P > 0.05$). There was no statistical difference in concordance rates for OLGA and OLGIM stages both for monozygotic and dizygotic twins.

**Conclusion**: Histological gastric mucosa alterations related to *H. pylori* gastritis and premalignant lesions in monozygotic and dizygotic twins show high rates of concordance.

M. Urba: None. L. Jonaitis: None. D. Janciauskas: None. L. Kupcinskas: None. J. Kupcinskas: None.

## P6.27 | Influence of *Helicobacter pylori* infection for the regulation of pro and antiapoptotic protein secretion in guinea pigs and cellular model

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**Introduction**: During *H. pylori* infection the interactions of bacterial components with gastric epithelial cells may result with deleterious effects due to cell apoptosis.

**Aim**: To evaluate the production of pro- or anti-apoptotic proteins in response to *H. pylori* components.

**Materials and methods**: Primary gastric epithelial cells of *Caviae porcellus* sensitive to *H. pylori* infection were propagated for 24 hours in the culture medium alone or with *H. pylori* antigens: glycine acid extract (GE), 10 μg/mL; cytotoxin-associated gene A (CagA) protein, 1 μl/mL; UreA urease subunit, 5 μg/mL; *H. pylori* or *Escherichia coli* lipopolysaccharide (LPS) 25 ng/mL or with live *H. pylori* CCUG17874

reference strain (2 hours, $2 \times 10^7$ CFU/mL). Animals were inoculated *per os* with *H. pylori* and 7/28 days later the infection and inflammation were assessed by histopathological, molecular (PCR) and serological examination. Cells or gastric tissue specimens were stained with antibodies to pro-apoptotic Bax/cleavage caspase 3 (CC3) or anti-apoptotic Bcl-xL/Bcl-2 proteins and with secondary FITC-labeled antibodies. Both in tissue and cell culture supernatants the concentration of matrix metalloproteinase (MMP)-9 was asses by ELISA.

**Results**: Pro-apoptotic CC3/Bax were detected in the gastric tissue of infected animals, 7/28 days after inculcation, whereas anti-apoptotic Bcl-xL/Bcl-2 proteins were diminished during the course of infection. Similarly, the level of CC3 was increased in primary gastric epithelial cells treated with *H. pylori* components whereas the expression of anti-apoptotic Bcl-2 was downregulated. Increased expression of pro-apoptotic proteins was correlated with elevated levels of MMP-9 in cell cultures and gastric tissue homogenates.

**Conclusions**: *H. pylori* components induce cell apoptosis, which may result in gastric barrier damage and upregulation of inflammatory response.

W. Gonciarz: None. A. Krupa: None. K. Hinc: None. M. Obuchowski: None. M. Chmiela: None.

## P6.28 | Leukocytes as a marker of immune response in experimental *in vivo* model of in *Helicobacter pylori* infection in guinea pigs model

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**Introduction**: *Helicobacter pylori* (HP) causes in humans gastritis/gastric or duodenal ulcers and cancers. The development of cellular immune response to infection remains unclear.

**Aim**: To estimate the initiation of immune response in *Caviae porcellus* (guinea pigs) exposed to HP on the basis of leukocytes distribution and antigen-specific proliferation of lymphocytes.

**Materials and methods**: Himalayan *Cavia porcellus* uninfected or infected with HP CCUG17874 VacA+/CagA+ ($10^{10}$ CFU/mL) were euthanized 7, 28 and 60 days after inoculation. The *H. pylori* status and inflammation in the stomach were confirmed by histological examination (Giemsa/Mayer's hematoxylin, eosin/silver staining), and the production of anti-HP antibodies. The blood smears were used for estimation of immunocompetent cells profile. The leucocytes, which were isolated from blood, spleen or lymph nodes, were incubated for 24 hours in the milieu of HP glycine acid extract-(GE)-10 μg/mL, phytohaemaglutinin-(PHA) 2 μg/mL or both EG/PHA. The cell proliferation was assessed by [3H]TdR incorporation.

**Results**: Chronic HP infection (28/60 days after inoculation) was accompanied by the systemic increase of eosinophils and lymphocytes, whereas in all infected animals the number of neutrophils in peripheral blood was decreased, which was correlated with an increased deposition of these cells in gastric tissue. HP infection in guinea pigs resulted in expansion of antigen specific lymphocytes (28/60 days after inoculations) localized in lymph nodes, which responded by proliferation to EG.

**Conclusions**: HP infection in guinea pigs was followed by the initiation of cellular innate and adaptive immune responses in association with deposition of neutrophils in gastric mucosa and systemic expansion of HP antigen-specific lymphocytes, respectively.

W. Gonciarz: None. A. Krupa: None. M. Chmiela: None.

## P6.29 | Role of Bcl-2 in regulation of endothelial cell apoptosis induced by *H. pylori* antigenic components

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**Introduction**: *Helicobacter pylori* (*HP*) is a Gram-negative bacterium, which adapts to acidic environment of human stomach, colonizes gastric mucosa then induces local and systemic inflammatory response. About 10% of infected individuals develop symptomatic gastritis, erosions, or peptic ulcers, while majority remain asymptomatic and develop chronic stage of infection. *HP*is considered a risk factor for cardiovascular disease, however, the mechanism linking an infection with atherogenic process is unknown. Previously we showed that *HP* components triggered ERK-dependent activation of endothelial cells, which led to cell apoptosis.

**Aim**: We asked whether endothelial cells were able to respond to pro-apoptotic activity of *HP* antigenic components. We evaluated the role of anti-apoptotic Bcl-2 protein, in regulation of endothelial cells apoptosis induced by *HP* antigens.

**Material and methods**: Primary aortal endothelial cells of *Caviae porcellus* were treated *in vitro* with selected *HP* components: glycine acid extract (GE) and lipopolysaccharide (LPS) for 6 and 18 hours. Bcl-2 expression was visualized by confocal microscopy after staining cells with anti-Bcl-2 antibodies, followed by FITC-conjugated secondary antibodies. The cell viability was estimated by MTT reduction assay and cell death analysis by nuclear staining with DAPI.

**Results**: The significant expression of Bcl-2 was detected in endothelial cells after 18 hours exposure to *HP* GE and LPS. The MTT reduction test indicated that endothelial cells after 72 hours of stimulation with *HP* components recovered and changed cell viability.

**Conclusions**: We suggest that endothelial cells exposed to *HP* antigens develop dysfunction of apoptosis and start repair process which might change endothelial homeostasis in the organism.

P. Rusek: None. A. Krupa: None. W. Gonciarz: None. M. Chmiela: None.

## P6.30 | Level active forms of oxygen in monocyte culture at lesions of stomach and duodenum associated with high dissemination *H. pylori* CagA(+) strains

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In herited disturbances of lectin way of complement activation are the risk factor of chronic contamination with highly pathogenic CagA strain of *Helicobacter pylori.*

**Aim of the research**: To determine of oxygen active forms in monocyte culture at lesions of stomach and duodenum associated with high dissemination *H. pylori* CagA(+) strains.

**Subjects and methods**: Monocyte culture of 56 subjects with erosive ulcer lesions of stomach and duodenum in the ages from 11 to 18 years. Tests for the presence of antibodies against CagA of *H. pylori* antigen, and concentrations of mannose-binding lectin and L-ficolin in blood plasma by immune enzyme method (Vector-Best, Russia). Oxygen active forms were determined in monocyte culture by chemiluminescent method.

**Results**: Secondary oxygen active forms in monocyte culture in patients with anti-CagA(+) antibodies showed increase intensity by 4 times ($P < 0.001$) in spontaneous process and increase intensity by 2.5 times ($P < 0.001$) in spontaneous process when studying the activity of primary radical of oxygen relative to patients without such. Discovered negative correlation isolated of reactive oxygen species with plasma concentration of mannose-binding lectin and L-fikolin ($r = -0.8$, $P = 0.03$; $r = -0.9$, $P = 0.002$). Thus an increase of dissemination with highly pathogenic strains is accompanied by higher stage of inflammatory activity and increased functional activity of monocytes, which are «professional» phagocytes.

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## P6.31 | Functional phagocytic activity in *Helicobacter pylori*-associated diseases

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Infection of the gastric mucosa *H. pylori* leads to the development of acute inflammation; neutrophils are the first to participate in the immune response of the body. The aim of the work was to study the functional activity of neutrophilic granulocytes and monocytes in patients with chronic (CG), chronic atrophic gastritis (CAG) associated with *H. pylori* infection. 85 patients with CG, 25 patients with CAG combined with *H. pylori* infection, and 100 practically healthy volunteers were examined. In all groups, the presence of *H. pylori* was detected by ELISA using the determination of the titer of specific antibodies to the CagA antigen of *H. pylori*. Activity of peripheral neutrophils and monocytes was assessed in a test with monodisperse latex particles by phagocytic index, phagocytic number, integral phagocytic index, and nitrosine-tetrazolium reduction reaction. The outcome of phagocytosis was determined by the state of oxygen-nondependent and oxygen-independent bactericidal systems using the nitro blue tetrazolium test and the total luminescence index of monocyte lysosomes. The adhesion and spreading of monocytes characterizing the state of their outer cytoplasmic membrane was investigated. Statistical data processing was carried out using the software packages Statistica for Windows 8.0. In all patients with CG and CAG with *Helicobacter pylori* infection, there was a decrease in the phagocytic activity of neutrophils and monocytes, which was combined with an increase in oxygen-nondependent and oxygen-dependent microbicidal mechanisms. The decrease in the ability of monocytes to adhere and spread in such patients reflects the functional state of the outer membrane of cells.

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## P6.32 | Distribution of IL-1B and IL-1RN alleles in *Helicobacter pylori* infected and non-infected dyspeptic patients

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**Aim**: To assess the distribution of IL-1B and IL-1RN polymorphism in *H. pylori* infected and non-infected dyspeptic patients.

**Background**: Interleukin 1B and Interleukin 1RN polymorphism influences host response to infection. The C→T at IL-B-511, and IL-1RN allele 2 have been implicated in host susceptibility to infection and varying gastric aliments. In this study, the alleles for IL-1B and IL-1RN in a local sample of dyspeptic patient with and without *H. pylori* infection have been investigated.

**Methods**: Biopsies of 52 dyspeptic patient were analyzed for SNP and (VNTRs) in IL-1B-511 and IL-1RN2 using PCR and restriction fragment length polymorphism. The frequencies of genotype were analyzed using Chi square test for independence to find the role of IL-1B and IL-1RN genotype with infection.

**Results**: The *H. pylori* prevalence was 65.3% in dyspeptic patients. Genotype TT in *H. pylori* non-infected patients turned out to be 66.6% whereas in infected patients it was 52.9%. IL-1RN2 found to be 17.6% among non-infected individuals as compared to 25.7% in

infected patients. The Chi square value was not significant for IL-1B-511 and IL-1RN genotype distribution.

**Conclusion**: In this study, all three alleles of IL-1B and three of the five reported alleles of IL-1RN were found in five out of fifteen possible combinations of genotype. The *H. pylori* infection found to be independent of IL-1B-511T and IL-1RN2. These results suggest that relationship between *H. pylori* infection and host genotype seems to be more complex and need to be further investigated.

N.S. Shakeel R. Farooqi: None.

## POSTER ROUND 6.3 MICROBIOLOGY AND GENOMICS OF HELICOBACTER

### P6.33 | Abundance and sequence variability of *Helicobacter pylori* prophages in the gastric niche of a pediatric population

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Phage sequences were recently identified in *Helicobacter pylori*, being present in about 20% of the strains. Generally these sequences are phage remnants most probably in a decay process. There is an agreement between the population structure of the bacterial host and the phage, pointing to a long last phage infection. Here we studied the genetic diversity of *H. pylori* prophages considering the whole genome sequence of 17 pairs of *H. pylori* isolated from the antrum and corpus of a pediatric population. We have found a surprisingly high intact prophage presence in the pairs of isolates (53%, 9/17). The prophage presence was consistent in both antrum and corpus of the same child. The percent identity between each pair ranged from 83.9% to 100%. Four pairs of prophages did not present single nucleotide polymorphisms (SNPs), while the remaining 5 pairs presented between 1 and 103 SNPs, counting in total 124 SNPs in 9 pairs. Of these we were able to identify 2 synonymous and 13 non-synonymous mutations and 4 SNPs in intergenic regions. Variant calling analysis revealed that some of these positions are polymorphic in each genome. The high proportion of intact prophages in *H. pylori* genomes (> 50%) may be due to chance, but it cannot exclude that prophages tend to be more frequent in the pediatric population, deserving further investigation. In this recently colonized pediatric population prophage pairs were highly similar among corpus and antrum isolates, although the presence of SNPs suggests a tendency for genetic diversification and niche adaptation.

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### P6.34 | Biological characterization of *Helicobacter pylori* outer membrane vesicles isolated by the biofilm and planktonic phenotypes

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*Helicobacter pylori* generates outer membrane vesicles (OMVs) during its growth in both planktonic and biofilm phenotypes. It has been demonstrated that OMVs are a component of *H. pylori* biofilm and that their interactions with associated extracellular DNA (eDNA) has a role in "bridging" OMV-OMV and OMV-cell interactions. The aim of the present study was the biological characterization of OMVs isolated by the planktonic (pOMVs) and biofilm (bOMVs) phenotypes at different timepoints, to elucidate the role of the OMVs in *H. pylori* growth and pathogenesis as a developmental process.

*H. pylori* ATCC 43629 biofilm formation was evaluated at 2, 6 and 10 days of incubation using confocal microscopy and live/dead staining and quantified image analysis. Enumeration of bOMVs and pOMVs associated with eDNA was performed using PicoGreen and PKH staining followed by flow cytometry acquisition. The bOMVs and pOMVs collected were subsequently analysed by nano LC-MS/MS to determine the exoproteome.

COMSTAT analysis showed no significant changes in thickness, biomass and roughness for each day, suggesting that biofilm reaches maturity after 2 days. Flow cytometry data demonstrated an increase of bOMVs and pOMVs over time and most of the detected vesicles (>60%) contained eDNA suggesting a possible key role of OMVs in eDNA delivery as well as in the biofilm formation. Proteomic analysis revealed a time and phenotype dependent modulation of many virulence related proteins, including the Vacuolating cytotoxin transporter which was 5 times more abundant in the biofilm, linking OMVs to virulence via biofilm formation.

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## P6.35 | Clarithromycin resistance in *Helicobacter pylori* under the magnifying glass of whole genome sequencing

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Clarithromycin-based triple therapy is prescribed worldwide for *Helicobacter pylori* eradication. However, increases in the clarithromycin resistance of *H. pylori* are leading to eradication failure of first line treatments containing this antibiotic. Resistance is mainly associated with three point mutations in two positions on the 23S rRNA structural domain V, being mutations A2142G and A2143G the most frequent, whereas mutation A2142C is less common. Recently, additional mutations have been reported, but their role in clarithromycin resistance is not yet clear. The aim of this study is to characterize point mutations in 23S rRNA gene of clarithromycin-resistant *H. pylori* strains. The genomes of 17 pairs of isolates from the antrum and corpus of a pediatric population were sequenced, and 23S rRNA sequences were aligned with MUSCLE. Seven pairs of isolates were resistant to clarithromycin, and six mutations were found: A2142G, A2142C, A2143G, T2182C, G2212A and T2244C. The A2143G is the most frequent point mutation (29.4% of patients for both antrum and corpus isolates), followed by A2142C/G and T2244C (5.9% in each mutation). Interestingly, antrum and corpus isolates from one patient showed the A2142C and A2142G mutation, respectively. Domain V was visually inspected after mapping reads to the assembled genome revealing variants in 94% of the genomes. Remarkably, 60% of the genomes of strains susceptible to clarithromycin exhibited variants matching mutations associated with clarithromycin resistance. Variant call analysis may provide complementary knowledge about the mechanism that leads to antibiotic resistance through the selection of less frequent variants by exposure to a selective agent.

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## P6.36 | VOC emission sampling from *Helicobacter pylori* cultures

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**Background**: Gastric cancer has a good chance to be cured if diagnosed at an early stage; the bacterial infection with *Helicobacter pylori* (*H. pylori*) is the main cause of gastric cancer and the related precancerous lesions. It is known that volatile organic compounds (VOCs) emitted in varying combinations and proportions by bacteria as metabolites, generate a characteristic odour for certain bacteria. These VOCs create a certain metabolic profile which can be used for species identification. Successful collection and identification of these metabolites can yield novel non-invasive diagnostic approaches.

**Methods**: The aim here was to identify a pattern of VOCs specific to *H. pylori*. To do this, we prepared a Columbia blood agar, within a sealable glass bottle, inoculated with *H. pylori* suspension and collected the headspace in sorbent tubes for downstream GC-MS, all while using VOC-neutral materials. In order to determine the optimal sampling time, VOCs were collected at various phases of growth where the bacteria differ by morphology and motility.

**Results and conclusions**: We have designed a collection system which allows us to capture the VOCs in sorbent tubes emitted from bacteria, cultivated in sealed, VOC-neutral containers while also maintaining a microaerobic environment. *H. pylori* here was cultivated on a solid media, but the methodology can be easily adapted for liquid cultures and varying atmospheric requirements.

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