5. Digestive pathophysiology (secretion, motility, permeability)

5.01 Expression of 17beta-hydroxysteroid dehydrogenase type 2 in normal, inflamed and neoplastic gastric mucosa

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Background: 17beta-hydroxysteroid dehydrogenases (17HSDs) are a group of enzymes regulating the concentrations of active sex steroids. 17HSD type 2 (17HSD 2) enzyme converts 17beta-hydroxysteroids into less potent forms. It is expressed in classical steroidogenic and steroid-responsive tissues, such as placenta, breast and endometrium. Recently, expression has been reported in absorptive epithelium of colon and small intestine where the potential function is in the inactivation of absorbed steroids. There are no reports about the expression of 17HSD 2 in human gastric mucosa.

Material and Methods: Gastric specimens from 45 patients (mean age 53, range 3-84; 24 females) were studied. 77 specimens included 17 with normal mucosa, 36 with inflammation and 23 with a neoplastic or dysplastic lesion. For expression studies, in situ hybridization with sense and antisense [a-35S]CTP-labelled probes for 17HSD 2 was used. The intensity and extent of expression were estimated.

Results: In normal gastric mucosa 17HSD 2 expression located in surface and foveolar epithelium, while in glandular epithelium the expression was weak or absent. Gender did not have any effect on the expression. However, there was some evidence for downregulation with age in non-inflamed mucosa (extent in gland neck; c=-0.69, p=0.02). Intestinal metaplasia showed an intense expression comparable to that found in intestine. Expression was downregulated in cancer as compared with both non-metaplastic and metaplastic epithelium (p<0.05).

Conclusions: A constant expression of 17HSD 2 is present in the gastric epithelium suggesting that steroid metabolism is a physiological function of the gastric mucosa. Downregulation associated with aging and gastritis might have some relevance in pathogenesis of gastric cancer. High expression in intestinal metaplasia mimics normal intestinal epithelium and might alter the local steroid metabolism.

5.02 Influence of different epidemiological, pharmacological and biological factors of serum pepsinogen levels

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Background: Serum pepsinogens I (sPGI) and II (sPGII) have been proposed from the early '80 as "serological biopsy" of gastric mucosa. Recently, the use of ELISA method instead of the radioimmunoassay labelling widely contributed to the spread of the test for the assessment of upper gastrointestinal disease, and particularly gastritis.

Methods: Four hundred and eighteen consecutive subjects (M190;F228, mean age 52, range15-102) admitted at the gastroenterological unit of Parma University as outpatients for an uninvestigated dyspepsia undergone a blood sample for serum pepsinogen determination (sPGI and sPGII): sex, age, Helicobacter pylori status (assessed by means of HpSA fecal antigen) in 121 subjects, PPs therapy, NSAIDs use, smoking habit and alcohol consumption. As normal values of sPGI and sPGII were considered 25-100 and 2-10 µg/l respectively.

Results: Sex: male, sPGI 140.7±8.3; sPGII 17.5±22.1. Female, sPGI 134.8±81.1; sPGII 16.2±3.7. Age <50: sPGI 129.3±73.8; sPGII 13.9±17.7. Age >50:sPGI 144.8±88.2; sPGII 19.4±22.9.

PPs use: sPGI 184.2±96.9; sPGII 20±14.7. No PPs: sPGI 115.5±64.3; sPGII 13.6±12.3 (<p<0.001). HP+ve: sPGI 137±76; sPGII 16±9; HP-ve: sPGI 98±48; sPGII 9±4. NSAIDs(+): sPGI 140.5±72.3; sPGII 15.3±15.4. NSAIDs(-): sPGI 120.9±65.5; sPGII15.2±14.5. Alcohol(-): sPGI 163.9±91.2; sPGII 16.9±13.4. Alcohol(+): sPGI 145.3±83.1; sPGII 17.3±15.0. Smokers: sPGI 144.8±75.9; sPGII 15.5±9.6. Not smokers: sPGI 143.3±91.0; sPGII 16.0±75.9.

Conclusions: sPGI and sPGII levels are mostly influenced by the Hp status as well as the antisecretory therapy with PPs. No modifications have been found as regards sex, smoking habit, NSAIDs use, alcohol consumption.

5.03 Does age affect gastric alcohol dehydrogenase (ADH) isoenzymes activities in H. pylori infected patients?

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Human gastric mucosa contains three ADH isozymes (class I, III and IV). The total gastric ADH activity is affected by a number of factors including age and infection of H. pylori. The partial impact of several ADH isoenzymes in this changes remains unliquidated.

Aim: To investigate the activity of ADH isoenzymes class I, III and IV in endoscopnic specimens of gastric mucosa from the patients of various age, considering H. pylori status.

Methods: The biopsy specimens of gastric body mucosa were taken from endoscopnic dyspeptic patient (29-63 years). The infection of Helicobacter pylori was confirmed with modified Giensa staining in 35 patients (age subgroup 50 years, n=9). The activity of class I, III and IV isozymes was measured using fluorimetric method with 4-methoxy-1-naphthaldehyde and of class III and IV isozymes using photometric method with n-octanol and m-nitrobenzaldehyde as specific substrates respectively.

Results: The activity of class I and III ADH did not differ significantly between infected and non-infected patients from each age subgroup. The activity of class IV ADH was significantly lower in H. pylori-positive specimens than H. pylori-negative: 12.3±3.54 vs. 16.25±2.51 for <40 year subgroup (p<0.02); 11.3±3.69 vs. 14.8±2.13 for 40-50 year (p<0.001); 8.89±2.68 vs.12.89± 3.06 U/mg of protein for >50 year subgroup (p<0.02). Summary. Helicobacter pylori infection leads to significant decrease (24-31%) of class IV ADH activity in gastric mucosa without any essential effect on class I and III ADH. The most reduced class IV isozyme activity was noted in H. pylori(+) patients older than 50 years.

Conclusion: Age of the patients >50 years accentuates the decrease of class IV gastric ADH activity in H. pylori(+) patients may be as a consequence of long lasting infection.

5.04 Serum pepsinogens and sucrase test in Helicobacter pylori related gastritis

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Background: Histology is still considered the golden standard for the diagnosis of H. pylori associated chronic gastritis and to evaluate the gastric mucosal damage. Serum pepsinogens I (sPGI) and II (sPGII), and gastric permeability investigated by oral sucrose test were found altered in chronic superficial and deep gastritis as well as in presence of atrophy.

Aim: To assess the integrity of gastric mucosa by two non-invasive tests: serum pepsinogen levels and oral sucrose test, and to investigate its relationship with histological findings.

Patients and Methods: A series of 24 consecutive out patients (12 females, 12 males; mean age 42 years, range 18-81) observed at our department for upper gastrointestinal symptoms were enrolled. All pa-
Patients were submitted to upper gastrointestinal endoscopy with biopsies examined by one pathologist according to the Updated Sydney System classification, and performed oral sucrose test using 40 mg in 100 ml of water; serum samples were analysed using panel test including of ELISA assays for sPGI and sPGII (Biohit, Helsinki, Finland). In first time, the patients were divided in Hp+ve and Hp -ve group and in second time in three groups: 1. normal histology, 2. superficial gastritis, 3. focal or diffuse atrophic gastritis.

Results: Fifteen patients resulted Hp +ve a statically significant difference was found between sPGI, sPGII and sucrose in Hp+ve patients compared with Hp-ve ones (sPGI 147.7± 52.0 vs 80.0±63.6 p=0.0006; sPGII 16.8±9.0 vs 7.4±2.5 p=0.007, sucrose 0.39±0.39 vs 0.07±0.06 p=0.007). A statically significant difference had been found for sucrose test singling out the patients according to different histological severity of damage: normal histology (7 patients): sucrose 0.07±0.07; superficial gastritis (10 patients): 0.34±0.41 and atrophic gastritis (7 patients): 0.37±0.39; p=0.06.

Conclusions: Serum pepsinogen I and II and sucrose test could be proposed as useful non-invasive methods to assess histological damage gastric mucosa, according to Hp status.

5.05 Does rebamipide, a gastroprotective agent, improve gastric permeability induced by Helicobacter pylori infection?

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Background: Helicobacter pylori infection and inflammation increase gastric mucosal permeability, and may develop chronic urticaria, migraine, atopic dermatitis and idiopathic thrombocytopenic purpura. Our aim was to evaluate the effect of a mucosal protective drug, rebamipide, on gastric mucosal permeability induced by Helicobacter pylori infection in human.

Patients and Methods: Permeability was measured by oral sucrose tolerance test. Twenty-five patients with H. pylori induced gastritis proven by endoscopy and 13C-urea breath test were entered to the study. They were given 30 mg of water within 15 min at fasting in the early morning before and after the treatment with rebamipide, 300mg/day for four weeks orally. Following that, urine was accumulated for 5 hours, and part was preserved at -80 deg C. Urinary sucrose concentration of all stored samples was measured using the Sucrose Evaluator Assay at one time. These results were corrected for by urine creatinine level and presented as mg/g CRE as an index of mucosal permeability.

Results: Urinary sucrose levels after administration of rebamipide were lower than those before treatment. H. pylori status was not significantly changed between before and after rebamipide treatment.

Conclusions: These results may induce the hypothesis that rebamipide has positive effect on gastric permeability in human.

5.06 Sucrose test and serum pepsinogens as markers of inflammation and damage in Helicobacter pylori related gastritis

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Background: Helicobacter pylori infection is characterized by activity in gastric mucosa. Serum pepsinogen I (sPGI) and II (sPGII) have been proposed as "serological biopsies" of gastric mucosa and resulted altered in Hp infection.

Aim: To evaluate sPGI and sPGII levels in relation to the topography of activity-induced Hp infection in gastric mucosa.

Patients and methods: Sixty-six consecutive out patients (36 F, 30 M mean age 45.7 years, range 18-88) referred to our department for dyspeptic symptoms were studied. In all patients, blood samples were taken to evaluate sPGI and sPGII levels (Biohit, Helsinki, Finland); each subject performed upper gastrointestinal endoscopy with five biopsies (2 antrum, 1 angulus, 2 corpus); gastritis was scored according to the updated Sydney System. We designed the topography of activity as antral-predominant activity (APA, antrum = corpus); gastritis was scored according to the updated Sydney System. We designed the topography of activity as antral-predominant activity (APA, antrum = corpus), corpus-predominant activity (CPA, corpus = antrum).

Results: Thirty patients were found Hp+ve and 36 Hp-ve. The topographical distribution of activity was described as APA in 14/30 of patients, DA in 12/30 and CPA in 4/30. Mean sPGI levels in Hp+ve were significantly higher compared with Hp-ve group (Hp+ve group: 9.5 µg/dl; APA: 14.2±2 µg/dl; DA: 12 µg/dl, p=0.0002). No differences was found comparing Hp+ve group with CPA: 18 µg/dl p=0.02. In the Hp+ve group, mean sPGII levels were higher in DA: 22 µg/dl vs APA: 14.2 µg/dl; without significant differences. Mean sPGI levels in Hp+ve were significantly higher in APA: 166 µg/dl and CPA: 150 µg/dl group compared to Hp-ve group: 101 µg/dl. No differences was found comparing Hp+ve group with CPA: 18 µg/dl group than in DA p=0.0003; sPGII levels result significantly lower in CPA: 71.5 µg/dl group than in DA p=0.0003.

Conclusion: These data confirmed that sPGII could be proposed as marker of activity induced by Hp infection; low levels of sPGI and sPGII can explain the presence of initial signs of mucosal damage.

5.07 Topography of gastric damage in H. pylori infection: evaluation by serum pepsinogens levels

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Background: Helicobacter pylori infection is characterized by activity in gastric mucosa. Serum pepsinogen I (sPGI) and II (sPGII) have been proposed as "serological biopsies" of gastric mucosa and resulted altered in Hp infection.

Aim: To evaluate sPGI and sPGII levels in relation to the topography of activity-induced Hp infection in gastric mucosa.

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Results: Thirty patients were found Hp+ve and 36 Hp-ve. The topographical distribution of activity was described as APA in 14/30 of patients, DA in 12/30 and CPA in 4/30. Mean sPGI levels in Hp+ve were significantly higher compared with Hp-ve group (Hp+ve group: 9.5 µg/dl; APA: 14.2±2 µg/dl; DA: 12 µg/dl, p=0.0002). No differences was found comparing Hp+ve group with CPA: 18 µg/dl p=0.02. In the Hp+ve group, mean sPGII levels were higher in DA: 22 µg/dl vs APA: 14.2 µg/dl; without significant differences. Mean sPGI levels in Hp+ve were significantly higher in APA: 166 µg/dl and CPA: 150 µg/dl group compared to Hp-ve group: 101 µg/dl. No differences was found comparing Hp+ve group with CPA: 18 µg/dl group than in DA p=0.0003; sPGII levels result significantly lower in CPA: 71.5 µg/dl group than in DA p=0.0003.

Conclusion: These data confirmed that sPGII could be proposed as marker of activity induced by Hp infection; low levels of sPGI and sPGII can explain the presence of initial signs of mucosal damage.