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PHOTOERADICATION OF HELICOBACTER PYLORI IN HUMANS: PHASE 1 STUDY

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In vitro studies show Helicobacter pylori (HP)can be killed with laser light after sensitisation with 5-amino laevulinic acid (5-ALA). In this first *in vivo* pilot study photodynamic eradication of HP was attempted in 7 healthy HP-positive (histology, breath test, urease test, culture) volunteers (26–46y, 5 males). Lansoprazole 30mg was given pre-irradiation. Ca. 45min after 5-ALA 20mg/kg p.o. a marked zone of antrum was irradiated with 410nm light (krypton laser) at an intensity of 100mW/cm^2 for 500s (50J/cm^2). In 2 patients a microlense diffuser and in 5 a cylindrical diffuser inside a balloon placed in contact with the mucosa were used. An adjacent zone of antrum was used as a control. Immediately, 2h and 48h after irradiation biopises for histology and culture were obtained. Fluoroscence measurements were performed before and after irradiation to assess photobleaching. **Results:** All 100%(n=7) patients were HP-positive by culture, urease & histology before irradiation. In the irradiated zone 4h and 48h post-irradiation 15% (1) and 28% (2) of patients were positive by culture and 15% (1) and 0% (0) were positive by histology, respectively. In the non-irradiated zone 50% (3) and 42% (3) were positive by culture and 42% (3) and 42% (3) by histology, respectively. Histology and culture concurred, except in 2 patients. Minimal histological thermal damage was seen in 28% (2) in the irradiated and in 15% (1) in the non-irradiated zones. Slight cutaneous photosensitisation (eythema) was seen in 3 subjects in the first 24h. **Conclusions:** HP was photoeradicated with low-dose 5-ALA in a specific zone of antrum in a majority of subjects with violet light and in about half with the white light of the gastroscope. These encouraging preliminary results will be followed up in further systematic studies. Supported by a research grant from Gruenenthal/Takeda AG

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EVALUATION OF A MODIFIED PYLORI-CHEK™/LARA® ^{13}C-UREA BREATH TEST PROTOCOL

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Background: The Pylori-Chek/LARA ^{13}C-urea breath test protocol uses an Ensure test meal, with breath samples collected 30 and 60 minutes. A fruit juice test meal results in earlier peak excretion of $^{13}CO_2$ compared with Ensure. Therefore, using fruit juice may allow the test to be shortened. **Aim:**To compare a modified protocol, using apple juice as the test meal and breath samples collected at 20 and 30 minutes, with the standard 60-minute protocol. **Methods:**Patients were tested by both protocols, in random order, on separate occasions. The standard protocol consists of a 273 ml Ensure test meal and breath samples collected at 30 and 60 minutes post-100 mg ^{13}C-urea ingestion. The modified protocol used a 155 ml apple juice test meal and 20- and 30-minute samples. The negative and positive cut-off values for excess $^{13}CO_2$ excretion ($\delta^{13}CO_2$) are $\leq$5.4 and $\geq$6.7, respectively. Results between these values are considered equivocal. **Results:** 88 patients had evaluable results for both protocols. 46 were negative by both, and 39 were positive. 1 patient was negative with juice and equivocal with Ensure. 2 patients were positive with juice, but equivocal (1) or negative (1) with Ensure. Therefore, for the 86 patients with definite results with the standard protocol, the sensitivity and specifity of the modified protocol was 100% and 98%, respectively. For the modified protocol, all 47 negative patients were negative at both time points. 1/39 of the positive patients was negative at 20 minutes ($\delta^{13}CO_2$=5.3). The median $\delta^{13}CO_2$ for positive patients was 18.0 at 20 minutes, and 21.5 at 30 minutes (p=0.3). **Conclusions:**The modified Pylori-Chek/LARA 13C-urea breath test protocol achieves comparable results to the standard protocol. Using apple juice as the test meal, it may be possible to further simplify the test to a single 20-minute post-urea breath sample.

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KNOWLEDGE OF UREASE TEST RESULT IMPROVES CULTURE RATE FOR HELICOBACTER PYLORI

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INTRODUCTION: Since antibiotic-resistant *H.pylori (Hp)* has emerged as a clinical problem, culture of *Hp* has resumed importance. This study was carried out to determine successful and cost effective strategies for routine culture of *Hp*. **METHODS:** Consecutive endoscopy patients agreed to give a total of 5 gastric biopsies for urease test (CLOtest), culture and histology. CLOtest was warmed after use for 3h, then kept at room temp until a final reading at 24h. Culture specimens were sent in 0.1ml saline to both the routine lab and the HP-lab to be cultured on 3 agar plates. Plates were incubated for 3–5 days at 37°C with 10% CO_2. In the HP-lab, half the biopsy was frozen at -85°C and used if the initial culture failed. Biopsies for histology from antrum and corpus were processed in H&E and Giemsa. If gastritis was noted but *Hp* was not, a silver stain was also performed. **RESULTS:** Of 268 patients, 110 were *Hp*-positive (41.04%). Overall the CLOtest was the most accurate with 265 patients correctly diagnosed (98.88%). In the two false negative tests *Hp*was detected only on histology. Histology was 100% sensitive but there were 4 false diagnoses. Culture was by definition 100% specific, but isolation rates varied between the labs. The difference was that the HP-lab staff knew the CLOtest result and could concentrate on probable positive specimens or could re-culture from frozen samples. **CONCLUSION:** In routine labs, culture success may be greatly improved if the urease test result is known. At $50 per *Hp*-negative case, $8,000 could have been saved if only urease positive biopsies were cultured.

%	CLOtest	Routine Lab	HP Lab	Histology
Sensitivity	98	75	95	100
Specificity	99	100	100	97

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HELICOBACTER PYLORI INHIBITS MUCIN SYNTHESIS IN GASTRIC MUCOUS CELLS: ROLE OF *VACA* AND *CAGA*

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Aim: The aim of this study was to investigate the effect of *H. pylori* on the function of gastric mucous cells and to study the role of the bacterial pathogenic factors *vagA* and *cagA*. **Methods:** *H. pylori* (10^4-10^7 CFU/well) was incubated with the mucin producing human gastric cell line HM02 for 12 and 24 hours. Mucin synthesis and secretion was determined by the incorporation of N-acetyl-[^{14}C]D-glucosamine into intracellular and released high molecular weight glycoproteins. *CagA* was analysed by RT-PCR and presence of vacuolating toxin was determined by incubation of HM02 cells with concentrated supernatants from *H. pylori* broth medium. **Results:** *H. pylori* impaired incorporation of N-acetyl-[^{14}C]D-glucosamine into intracellular glycoproteins. Significant inhibition of mucin synthesis was noted after 12 and 24 h cocultivation with a bacterial load of $\geq 10^5$ bacteria (bacteria/cell ratio = 0.25). The amount of secreted mucins from HM02 cells treated with *H. pylori* remained unchanged. There was no significant variation in cell number between *H. pylori*-infected cells over the 24 h incubation period.The *cagA* positive and cytotoxin producing strains (HP64, HP57 and HP87) produced 1.8 fold stronger inhibition of intracellular mucin synthesis than the *cagA* negative, non-cytotoxin producing strains (HP05, HP83 and HP84). In contrast to *H. pylori,* C. *jejuni* stimulated incorporation of N-acetyl-[^{14}C]D-glucosamine into intracellular mucins. **Conclusion:** The results indicate that *H. pylori* directly impairs mucin synthesis in gastric mucous cells. The enhanced effect of cytotoxic strains on mucin synthesis can be considered as one possible factor responsible for the increased risk to develop peptic ulceration with these strains.

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HELICOBACTER PYLORI AUGMENTS THE INHIBITORY EFFECT OF OMEPRAZOLE IN GASTRIC H^+K^+-ATPASE MEMBRANE VESICLES

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Background: In duodenal ulcer patients intragastric acidity during omeprazole treatment is significantly lower before *H. pylori* eradication than after cure. The aim of this study was to examine whether *H. pylori* alters the inhibitory characteristics of omeprazole at the level of the H^+/K^+-ATPase. **Methods:** Pig gastric membrane vesicles enriched in H^+/K^+-ATPase activity were incubated with *H. pylori* (intact bacteria and sonicate) and the *H. pylori* fatty acid cis 9,10-methyleneoctadecanoic acid (MOA); the inhibitory effects of omeprazole on proton transport were monitored fluorometrically by the pH sensitive dye acridine orage. The number of thiol groups associated with the vesicle protein was determined with 5,5'-dithiobis(2-nitrobenzoic acid). **Results:** H^+/K^+-ATPase mediated proton transport in gastric vesicles was inhibited by omeprazole in a time- and pH-dependent manner. In gastric membranes vesicles pretreated with *H. pylori, H. pylori* sonicate or MOA the onset of the inhibitory action of omeprazole and the proton efflux out of the vesicles was enhanced. Furthermore, *H. pylori* increased the number of accessible thiol groups in the vesicle membrane and increased membrane permeability. **Conclusion:** Our results show that *H. pylori* enhances the inhibitory effect of omeprazole at the H^+K^+-ATPase level. The data are consistent with the hypothesis that *H. pylori* increases the affinity of the omeprazole cyclic sulfenamide to the proton pump by unmasking target thiol groups and/or acceleration of drug entry into the H^+K^+-ATPase.