# PROGRAM AND ABSTRACTS

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ON

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AND

### **CHEMOTHERAPY**

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710 In vitro antibiotic susceptibility of Rochalimaea isolates of the three species R. quintana, R. vinsonii, and the novel species R. henselae.

M.MAURIN, D.RAOULT. Centre National de Référence pour les Rickettsioses, Marseille, France.

We have evaluated the antibiotic susceptibilities of three Rochalimaea species: R. quintana (Fuller strain, ATCC VR-358), and R. vinsonii (Baker strain, ATCC VR-152) obtained from G.A.Dasch (Naval Medical Research Institute, Bethesda, MD), and a human isolate of R. henselae, the agent of bacillary angiomatosis in patients with AIDS, obtained from the CDC. The dilution susceptibility testing method in Mueller Hinton agar supplemented with 5 % sheep blood was used. Since the Rochalimaea agents are fastidious gram negative bacteria, the growth was evaluated on days 3, 5, and 7 of the antibiotic experiments, by comparison to drug-free agar controls. The study shows that all three isolates were highly susceptible to penicillin G, amoxicillin, and third generation cephalosporins, the tetracyclines, rifampin, and the macrolides including azithromycine and clarithromycine. The MIC 100% ranged from less than 0.125 to 0.25 after 5 days incubation of the plates. Aminoglycosides were also effective with MIC 100% ranging from less than 0.125 to 2. MIC 100% of chloramphenicol ranged from 1 to 4. Among the fluoroquinolones, sparfloxacin and ciprofloxacin were the most potent, with MIC 100% of 0.25 to 1. The contrast between in vitro antibiotic susceptibility data and the poor efficacy of antibiotic treatment in infected patients has still to be explained. The possibility that cell association of the Rochalimaea agents, which was shown in vitro in cell cultures, may impair antimicrobial activity, has to be evaluated.

711 Seroprevalence of <u>Helicobacter pylori</u> IgG antibodies in Canadian Children. B. DEMERS\*, M. KARMALI, P. SHERMAN. The Hospital for Sick Children, Toronto.

Serological studies have helped define the prevalence of H. pylori infection in different populations. The prevalence of H. pylori IgG is low during childhood, and increases with age so that about half the population in industrialized countries is seropositive by age 20-60 yrs. The aim of our study was to evaluate the seroprevalence of H. pylori IgG in Canadian children, information which has hitherto not been available. This was done by using a new commercial ELISA method (Joldon Diagnostics, Ontario). We tested sera from 200 otherwise healthy children whose samples were submitted for investigation of acute respiratory infections. They comprised 10 from patients aged 0 - 6 m., 10 from those aged 6 m. to 1 yr., and 10 samples from each ensuing one year age group from 1 - 18 yrs. inclusively. We also tested sera from 10 children with dyspepsia who were culture-positive in antral biopsies for H. pylori and 10 who were culture-negative. The sera were tested in triplicate at a dilution of 1:100. The test was reliable and reproducible. Using the mean ELISA values (MEV's) of the negative sera plus 2SD as a cut off value (50.0), the sensitivity, specificity, positive predictive value, and negative predictive values were each 90%. The MEV in the 200 control sera ranged from 0-273.3; the values were distributed in a positively skewed manner with a median MEV of 20 and a mean of 31.6. The MEV of sera from 10 H. pylori culture-positive patients was 152.2 (range 49.0-312.8) and that from the 10 culture-negative cases was 22.4 (range 7.4-52.7), ip <0.01. The overall frequency of H. pylori IgG in the 200 control sera was 15%, the aged-related frequency being 20% (0-6 m.), 0% (6 m. - 1 yr), 6% (1-5 yrs), 20% (6-10 yrs), and 18.75% (11-18 yrs). The relatively high frequency of H. pylori IgG in young infants (0 - 6 m.) likely reflects maternal antibody.

712 Does the Success of Anti-Helicobacter pylori
(HP) Therapy Depend on a Direct Antimicrobial
Effect of TDB? A MCKINLAY, K MILNE and I
GOULD\* Aberdeen Royal Infirmary, Aberdeen. U.K.

It is usually assumed that Tripotassium-dicitratobismuthate (TDB) functions as an antimicrobial against HP. Most studies have examined the bacteriostatic effects of drugs but the outcome of anti-HP therapy may depend on bactericidal activity. We have developed a microtitre method enabling full time kill studies to be performed on all 64 combinations in a checkerboard and used this to study 4 strains of HP. TDB + Tetracycline (Tc) and TDB + Amoxycillin (Am) produced little antibacterial activity at 4 and 8 hrs, but killing was complete by 24 hrs with any combination containing 0.0625ug/ml of Am or 8ug/ml of Tc. The contribution from TDB was minimal, at concentrations up to 128ug/ml. In contrast, with Metronidazole (Mz) + TDB a bactericidal effect was seen at 8 hrs in any well containing lug/ml Mz. Again the effect of TDB was minimal. There was no evidence of synergy with any of the combinations tested, and TDB appeared to contribute little to the overall activity. Both Tc and Am were bactericidal at 24hrs, but their speed of kill slow. Mz had a more rapid onset of action against HP, and this may explain why it has proved more effective in vivo.

Our results suggest the success of combination therapy may not be due to a direct antimicrobial effect of TDB.

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Effect of pH Variation on the Susceptibility of <u>Kelicobacter pylori</u> to Three Hacrolide Antimicrobials and Temafloxacin.

G.J. MALANOSKI\*, G.M. ELIOPOULOS, M.J. FERRARO, and R.C. MOELLERING, JR. New England Deaconess and Massachusetts General Hospitals, Harvard Medical School, Boston, MA

The in vitro susceptibility of 27 clinical isolates of <u>**Kelicobacter**</u> pylori to erythromycin, clarithromycin, azithromycin, and temafloxacin under various pH conditions was evaluated. Clarithromycin (MIC<sub>90</sub>=0.03 ug/ml) was found to be significantly more active than either erythromycin (MIC $_{90}$ =0.125 ug/ml) or azithromycin (MIC<sub>90</sub>=0.25 ug/ml) at a neutral pH. Lowering the pH to resulted in a loss in efficacy from 8 to 32 fold for all three macrolides studied. However, the  ${
m MIC}_{90}$  of clarithromycin (0.5 ug/ml) remained well within clinically achievable serum concentrations and lower than those of azithromycin (2 ug/ml) and erythromycin (4 ug/ml). Temafloxacin alone was active (MIC=0.25-2 ug/ml) at a neutral pX but also became less effective at the lower pH. No synergism or antagonism was observed with combinations of clarithromycin and temafloxacin at either the neutral or lower pH ranges. Relative preservation of in vitro activity at a reduced pX may influence favorably the in vivo efficacy of clarithromycin in the treatment of peptic ulcer disease associated with Helicobacter pylori, since the local pH of the gastric mucosa may vary considerably.

714 High resistance of Helicobacter pylori to metronidazole in Mexico. S.RANGEL-FRAUSTO\*, S.ALOR, Y.LÓPEZ-VIDAL, J.J.CALVA AND G.M.RUIZ-PALACIOS. National Institute of Nutrition, Mexico City, Mexico.

Helicobacter pylori infection has been associated with duodenal ulcer. Treatment requires nutlitherapy with active antimicrobial agents; imidazole derivatives are the cornerstone in the treatment of H. pylori infections, and the failure to eradicate the organism is related to drug resistance. Since metronidazole is overprescribed for diarrhea in Mexico. H pylori resistance to this drug may be high.

We studied the susceptibility patterns to 18 antibiotics, of *H. pylori* isolated from Mexican adults. Eighteen isolates from patients with epigastric pain and endoscopically proven duodenal ulcer were included in this study. *H. pylori* status was assessed by culture, histology and urease test using antral biopsy specimens. *H. pylori*-associated antral gastritis was diagnosed in all patients. The agar dilution method was used to determine minimum inhibitory concentration (MICs) of erithromyein, ampieillin, amoxicillin, penicillin, cephalotin, cefotaxime, chloramphenicol, nitrofurantion, tetraeyeline, doxiciclyne, rifampin, amikacin, gentanicin, tobramicin, metronidazole, ciprofloxacin, norfloxacin, and bismuth subsalicylate against *H. pylori* strains. A control strain (*H pylori* CCUG15818) was used.

H pylori was found highly susceptible to all aminoglycosides, B-lactarns, quinolones and tetracyclines; 50% of strains were resistant to metronidazole (MIC $_{90}$  32 ug/mL). The sensitivity to bismuth salts was moderate, with an MIC $_{90}$  of 32 ug/mL.

The high misuse and overprescription of metronidazole may explain the selection of H. pylori resistance to this drug in this Mexican population.

715 Evaluation of the QuickVue EIA Test for the Detection of Helicobacter pylori IgG Antibodies in Documented Cases of H. pylori Infections. S. HOFFMAN\*, L.J. BARRETT, Z.J.

YU, B.J. MARSHALL and R.L. GUERRANT. University of Virginia, Charlottesville, VA.

Helicobacter pylori (HP) intection is becoming increasingly important in the management of gastritis and peptic ulcer disease. Proof of infection requires an expensive and invasive endoscopic procedure. QuickVue (QV) is a rapid enzyme immunoassay test for the qualitative detection of IgG antibodies specific to HP in serum or plasma. In this study, 30 patients with biopsy proven HP infection (HP-pos) and 30 without HP (HP-neg) were tested in duplicate using the QV test by two investigators blinded to patient status and each other's test results. 13 of 120 tests which gave no color reaction after the 5 minute incubation period were centrifuged and retested resulting in 12/13 correct results and one faint blue "equivocal" (E) reaction from a HP-pos patient. The table below summarizes results of 120 tests in 60 patients (30 HP-pos, 30 HP-neg).

QV by 2 investigators	HP-pos (30)	HP-neg (30
Both HP-pos	28	1
One HP-pos and one Equivocal	2	1
One HP-pos and one HP-neg	0	3
One HP-neg and one Equivocal	0	7
Both E	0	1
Both HP-neg	0	17

In conclusion, the QuickVue assay would be a convenient screening assay. With an overall sensitivity of 97% and negative predicative value of 96%, a negative result on QV suggests there is no need for further testing for HP. However, positive or equivocal results require additional confirmation (ie. qualitative ELISA, breath test, or biopsy).